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(54) Title: USE OF SPECIFIC BINDING MOLECULES IN POTENTIATING IGF-I ACTIVITY

(57) Abstract

Antibodies and other specific binding molecules which bind to insulin-like growth factor-I (IGF-I), particularly the 1-17, 18-21, 22-37, 45-53, 54-60, 59-70 or, especially, the 36-44 region, potentiate or enhance its activity. The antibodies may be generated *in situ* by administering an appropriately antigenic molecule. IGF-I potentiation is useful in a wide range of clinical conditions.

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USE OF SPECIFIC BINDING MOLECULES IN POTENTIATING IGF-I ACTIVITY

This invention relates to specific binding molecules, means for generating them, and their use to potentiate or enhance one or more biological activities of insulin-like growth Factor I.

Insulin-like growth factor-I (IGF-I) is a potent peptide hormone (molecular weight of approximately 7,500 kDa) which is thought to mediate many of the anabolic actions of growth hormone (GH) as well as having independent actions to stimulate cell hyperplasia, hypertrophy and differentiation (Daughaday and Rotwein, *Endocrine Reviews* **10** 68-92 (1989)). IGF-I is synthesised by many tissues in the body and may therefore exert local autocrine/ paracrine actions; in addition, the liver secretes large amounts of IGF-I into the blood where it can have widespread endocrine actions on peripheral tissues. IGF-I usually binds with high affinity to type 1 receptors, which are thought to mediate most of its actions. However, it can also bind weakly to insulin and type 2/mannose-6-phosphate receptors.

Only very small amounts of IGF-I are found as free peptide *in vivo*. Instead, it is bound to binding proteins (IGFBPs) of which six high affinity proteins have been characterised so far (Sara and Hall, *Physiological Reviews* **70** 591-614 (1990)). The precise function of this complex arrangement of IGFBPs with IGF-I is unknown at present but several options have been suggested: neutralisation of the "insulin like" actions of IGF-I, inhibition of general IGF-I activity, transport of IGF-I from blood to tissues or from one cell type to

another, targeting of IGF-I towards tissue receptors, maintenance of the IGF-I pool. Most experiments to date, both *in vivo* and *in vitro*, have indicated that IGFBPs are inhibitory for IGF-I action, although some reports have demonstrated enhancement of IGF-I activity *in vitro* (Elgin *et al*, *Proceedings of the National Academy of Sciences of the USA*, **84** 3254-3258 (1987); and Conover, *Endocrinology* **130** 3191-3199 (1992)). This apparent potentiation of IGF-I action is thought to be due to the adherence of the IGFBPs to cell surfaces thus presenting IGF-I to its receptor; decreased affinity of the BPs for IGF-I may also be involved, allowing receptors to compete more effectively for IGF-I.

WO-A-8908667 and WO-A-8909268 both disclose the production of recombinant IGFBPs; the former additionally discloses enhancement of IGF-I activity by the recombinant protein.

Some structural properties of IGF-I have been identified. IGFBPs generally bind to residues 1-18 and 49-51 of IGF-I. Des(1-3) IGF-I and long-R IGF-I, which are IGF-I analogues that bind poorly to IGFBPs, exhibit increased activity compared with IGF-I alone both *in vivo* and *in vitro* (Tomas *et al*, *Biochemical Journal* **282** 91-97 (1992)). Type 1 receptor activity and binding is associated with residues 22-37 (equivalent to the C-peptide region of pro-insulin). Type 2 receptor binding is in the region of residues 49-58. The function of the C-terminal D-loop is unknown.

Polyclonal and monoclonal antibodies against IGF-I are known. EP-A-0292656, for example, discloses monoclonal antibodies against IGF-I and their use in an immunometric

assay for IGF-I. As far as the effect of such antibodies on IGF-I activity is concerned, all IGF-I binding antibodies studied to date (monoclonal or polyclonal) have either inhibited IGF-I activity or had no demonstrable effect on IGF-I action. For example, studies demonstrating inhibitory action of anti-IGF-I antibodies include the following:

Schlechter *et al*, *American Journal of Physiology* **250** E231-E235 (1986);

Ooi and Herington, *Biochemical and Biophysical Research Communications* **156** 783-791 (1988);
Gluckman, Disclosure at the Second International Conference on IGFs at San Francisco on January 12th to 16th 1991 and submitted to *J. Endocrinol* (1991);
Mondschein *et al*, *Biology of Reproduction* **40** 79-85 (1989);
Morrell *et al*, *J. Molec. Endocrinol.* **2** 201-206 (1989) and
Bicsak *et al*, *Endocrinology* **126** 2184-2189 (1990).

The following studies demonstrate no apparent action of anti-IGF-I antibodies:

Kerr *et al*, *J. Endocrinol.* **124** 403-415 (1990) and
Spencer *et al*, *Endocrinology* **128** 2103-2109 (1991)

To complete this brief survey of the known literature, Tamura *et al*, *J. Endocrinol.* **125** 327-335 (1990) did not draw any conclusions on the action of specific anti-IGF-I antibodies studied.

It has now been found that it is in fact possible to enhance the *in vivo* activity of endogenous or exogenous IGF-I by antibody binding, or by the binding of other specific binding molecules. Furthermore, the fact that the observed enhancement is not confined to natural IGF binding proteins shows that there is apparently a different mechanism at work from that previously proposed in the observations on IGFBPs.

According to a first aspect of the invention, there is provided a specific binding molecule, other than a natural IGF binding protein, which is capable of binding to insulin-like growth factor-I (IGF-I) and which is capable of enhancing a biological activity of IGF-I.

The term "specific binding molecule" as used in this specification includes natural antibodies (whether polyclonal or monoclonal), antibody fragments and modified and chimeric antibodies (including humanised antibodies), all of which have antigen (in this case IGF-I) binding capability, as well as other, non-antibody-derived, specific binding molecules. Such other specific binding molecules include wholly or partially synthetic peptides and proteins (which terms include glycopeptides and glycoproteins where the context so admits), natural and modified receptors for IGF-I and modified molecules based on, for example, natural binding proteins for IGF. (In this context, "modified" molecules include those which have a substantial homology, such as more than 60, 80 or 90%, with the corresponding natural molecule; a "modified" molecule may alternatively contain an IGF-I binding region which has substantial homology with the corresponding region of a natural molecule.) For many applications, antibodies and antibody-derived molecules

will be preferred, not least for th ir ease of availability and/or preparation and their familiarity to those skilled in the art. Polyclonal and monoclonal natural antibodies may be chief amongst those preferred, but humanised antibodies (for example as taught by Winter and Milstein (*Nature* **349** 293-299 (1991)) may be as suitable, or even optimal, in certain circumstances.

The specific binding molecule, whatever its nature, is capable of enhancing at least one biological activity of IGF-I. Such an activity may, but will not necessarily be an IGF-I-mediated anabolic action of growth hormone.

IGF-I has been shown to have wide reaching actions and therefore this invention could have applications for animal growth and biotechnology, veterinary practice and clinical medicine. IGF-I can stimulate or improve the processes listed below and therefore enhancement of IGF-I activity has similar applications. In particular, therefore, the (or one of the) biological activities of IGF-I may include:

Increasing whole body and muscle growth rate in normal and hypopituitary animals (Schoenle *et al*, *Nature* **296** 252-253 (1982), and Hizuka *et al*, *European Journal of Pharmacology* **125** 143-146 (1986));

Protection of body weight and nitrogen loss during catabolic states (such as fasting, nitrogen restriction, elevated corticosteroid levels and/or diabetes) (Ballard *et al*, "Effects of IGF-I and IGF analogues on growth during catabolic states in rats" In: Modern Concepts of Insulin-like Growth Factors,

pp 617-627. Ed., Spencer, E.M. Elsevier: New York (1991));

Kidney regeneration (Flyvbjerg *et al*, "Kidney IGF-I accumulation occurs in four different conditions with rapid initial kidney growth in rats" In: Modern Concepts of Insulin-like Growth Factors, pp 207-217. Ed., Spencer, E.M. Elsevier: New York (1991));

Nerve regeneration (Komoly *et al*, *Proceedings of the National Academy of Sciences USA* **89** 1894-1898 (1992));

Hypoxia (Gluckman *et al*, *Biochemical and Biophysical Research Communications* **182** 593-599 (1992));

Wound healing (Mueller *et al*, "The role of IGF-I and IGFBP-3 in wound healing" In: Modern Concepts of Insulin-like Growth Factors, pp 185-192. Ed., Spencer, E.M. Elsevier: New York (1991)); and Jennische *et al*, "Local expression of somatomedins during tissue growth and regeneration" In: The Insulin-like Growth Factors, Structure and Biological Functions. Ed. Schofield, P. CRS: Oxford (in press) (1991));

Cardiac regeneration (Florini *et al*, "Proteins induced by the IGFs in skeletal, smooth and cardiac muscle: implications for cardiovascular diseases" In: Modern Concepts of Insulin-like Growth Factors, pp 487-503 Ed., Spencer, E.M. Elsevier: New York (1991));

Cancer cachexia (Ng *et al*, *American Journal of Physiology* **262**(3) R426-R431 (1992));

Angiogenesis (Nakaohayashi *et al*, *Atherosclerosis* **92** 141-149 (1992));

Regeneration of the gastrointestinal tract (Vanderhoof *et al*, *Gastroenterology* **102** 1949-1956 (1992));

Stimulation of mammary function (Peri *et al*, *Cell Biology International Reports* **16** 359-368 (1992));

IGF-I-dependent actions of GH (such as, usefulness in metabolic stress, age-related decreases in GH activity and adult GH deficiency) (M. Keliman, *Journal of the American Geriatrics Society* **39** 295-307 (1991); F.E. Kaiser, *Geriatrics* **47** 85 (1992); Chwals and Bistrian, *Critical Care Medicine* **19** 1317-1322 (1991); and Sonksen *et al*, *Acta Paediatrica* **S379** 139-146 (1991));

Usefulness in maturity-onset diabetes (Schalch *et al*, "Short-term metabolic effects of recombinant human insulin-like growth factor I (rhIGF-I) in type II diabetes mellitus" In: Modern Concepts of Insulin-like Growth Factors, pp 705-713 Ed., Spencer, E.M. Elsevier: New York (1991)); and/or

Usefulness in specific IGF-I deficiency (Laron dwarfism) (Laron *et al*, *Lancet* **339**(8804) 1258-1261 (1992)).

Neither the above nor any other medical utilities for specific binding molecules for IGF-I (including IGF binding proteins) has been suggested. According to a second aspect of the invention, therefore, there is provided a specific binding molecule which is capable of binding to insulin-like growth factor-I (IGF-I) and which is capable of enhancing a biological activity of IGF-I, for use in medicine. In this aspect of the invention, natural IGF binding proteins may be used.

The complete amino acid sequence of mature, human IGF-I is as follows (SEQ ID NO: 1):

```
1           11          21          31
GPETLCGAEL  VDALQFVCGD  RGFYFNKPTG  YGSSSRRAPQ

41          51          61
TGIVDECCFR  SCDLRRLEMY  CAPLKPAKSA.
```

Among the regions of IGF-I to which specific binding molecules in accordance with the invention may bind is included at least part of the region encompassing residues 1 to 17, and particularly 11 to 17, as numbered above from the N-terminus of mature IGF-I. Other preferred regions include those encompassing residues 18 to 21, 45 to 53, 54 to 60 and, especially, 36 to 44. Further preferred regions include those encompassing 22 to 37 and 59 to 70. The specific binding molecules need not bind to all of such a preferred region; however, a peptide fragment of some or all of this (or any other) preferred region of IGF-I may bind, for example competitively with IGF-I itself to specific binding molecules within the invention. It should be stressed that other r gions of IGF-I may also be preferred as epitopes for molecules of the invention, while some for

preference should be avoided. It is much pr ferred, though, that the specific binding molecules of the invention do not bind to other, or other significant, proteins,especially IGF-II or insulin, with both of which IGF-I shares some characteristics.

It has been stated above that antibodies are among the specific binding molecules preferred for use in the invention. One particularly convenient way of ensuring a plentiful supply of antibodies is to generate them *in situ*. This can be achieved by administering to a (generally human) subject an appropriate antigenic molecule.

According to a third aspect of the invention, there is therefore provided an antigenic molecule which is capable, upon (generally parenteral) administration to a subject, of causing the generation of antibodies, wherein the antibodies are capable of binding to insulin-like growth factor-I (IGF-I) and of enhancing a biological activity of IGF-I.

Suitable antigenic molecules may (but will not necessarily) be based on peptide fragments, for example those corresponding to a region of IGF-I to which binding is sought. On this basis, a suitable antigenic molecule may be based on a fragment encompassing some or (preferably) all of residues identified above as being preferred (and possibly no significant other fragment sequence of IGF-I). Whether or not specifically so based, a preferred antigenic molecule in accordance with this aspect of the invention causes antibodies to be raised against at least some of the above-identified residues of IGF-I.

Short p ptides will not as a rule be antigenic in their own right, although they can confer epitope specificity. They may be rendered antigenic by a variety of means, such as those disclosed in WO-A-8900166. Essentially, they may be coupled to carrier molecules, such as albumin, by coupling agents (such as glutaraldehyde), to form a suitable antigen molecule. Of course, equivalent and other antigenic molecules containing the peptide fragment of interest may be synthesised by recombinant DNA technology, or even chemically.

Suitable short peptides on which antigenic molecules may be based include, but are not limited to, hexamers, heptamers and octamers. Hexameric peptides derived from the regions of IGF-I identified as preferred include:

(those including at least four residues from, and preferably wholly within, the 1-17 region, GPETLCGAELVDALQFV) (SEQ ID NO: 2)

GPETLC (SEQ ID NO: 3)
PETLCG (SEQ ID NO: 4)
ETLCGA (SEQ ID NO: 5)
TLCGAE (SEQ ID NO: 6)
LCGAEL (SEQ ID NO: 7)
CGAELV (SEQ ID NO: 8)
GAELVD (SEQ ID NO: 9)
AELVDA (SEQ ID NO:10)
ELVDAL (SEQ ID NO:11)
LVDALQ (SEQ ID NO:12)
VDALQF (SEQ ID NO:13)
DALQFV (SEQ ID NO:14)
ALQFVC (SEQ ID NO:15)
LQFVCG (SEQ ID NO:16)

(those encompassing the 18-21 region, CGDR) (SEQ ID NO:17)
FVCGDR (SEQ ID NO:18)
VCGDRG (SEQ ID NO:19)
CGDRGF (SEQ ID NO:20)

(those including at least four residues from, and preferably wholly within, the 22-37 region,

GFYFNKPTGYGSSSRR) (SEQ ID NO:21)
DRGFYF (SEQ ID NO:22)

RGFYFN (SEQ ID NO:23)
GFYFNK (SEQ ID NO:24)
FYFNKP (SEQ ID NO:25)
YFNKPT (SEQ ID NO:26)
FNKPTG (SEQ ID NO:27)
NKPTGY (SEQ ID NO:28)
KPTGYG (SEQ ID NO:29)
PTGYGS (SEQ ID NO:30)
TGYGSS (SEQ ID NO:31)
GYGSSS (SEQ ID NO:32)
YGSSSR (SEQ ID NO:33)
GSSSRR (SEQ ID NO:34)
SSSRRA (SEQ ID NO:35)
SSRRAP (SEQ ID NO:36)

(those including at least four residues from, and preferably wholly within, the preferred 36-44 region, RRAPQTGIV) (SEQ ID NO:37)
SSRRAP (SEQ ID NO:38)
SRRAPQ (SEQ ID NO:39)
RRAPQT (SEQ ID NO:40)
RAPQTG (SEQ ID NO:41)
APQTGI (SEQ ID NO:42)
PQTGIV (SEQ ID NO:43)
QTGIVD (SEQ ID NO:44)
TGIVDE (SEQ ID NO:45)

(those including at least four residues from, and preferably wholly within, the 45-53 region, DECCFRSCD) (SEQ ID NO:46)
IVDECC (SEQ ID NO:47)
VDECCF (SEQ ID NO:48)
DECCFR (SEQ ID NO:49)
ECCFRS (SEQ ID NO:50)
CCFRSC (SEQ ID NO:51)
CFRSCD (SEQ ID NO:52)
FRSCDL (SEQ ID NO:53)
RSCDLR (SEQ ID NO:54)

(those including at least four residues from, and preferably wholly within, the 54-60 region, LRRLEMY) (SEQ ID NO:55)
CDLRRL (SEQ ID NO:56)
DLRRLE (SEQ ID NO:57)
LRRLEM (SEQ ID NO:58)
RRLEMY (SEQ ID NO:59)
RLEMYC (SEQ ID NO:60)
LEMYCA (SEQ ID NO:61)

Heptameric peptides derived from the regions of IGF-I identified as preferred include:

(those including at least four residues from, and preferably wholly within, the 1-17 region, GPETLCGAELVDALQFV) (SEQ ID NO: 2)
GPETLCG (SEQ ID NO:62)
PETLCGA (SEQ ID NO:63)
ETLCGAE (SEQ ID NO:64)
TLCGAEL (SEQ ID NO:65)
LCGAELV (SEQ ID NO:66)
CGAELVD (SEQ ID NO:67)
GAELVDA (SEQ ID NO:68)
AELVDAL (SEQ ID NO:69)
ELVDALQ (SEQ ID NO:70)
LVDALQF (SEQ ID NO:71)
VDALQFV (SEQ ID NO:72)
DALQFVC (SEQ ID NO:73)
ALQFVCG (SEQ ID NO:74
LQFVCGD (SEQ ID NO:75)

(encompassing the 18-21 region, CGDR) (SEQ ID NO:17)
QFVCGDR (SEQ ID NO:76)
FVCGDRG (SEQ ID NO:77)
VCGDRGF (SEQ ID NO:78)
CGDRGFY (SEQ ID NO:79)

(those including at least four residues from, and preferably wholly within, the 22-37 region, GFYFNKPTGYGSSSRR) (SEQ ID NO:21)
GDRGFYF (SEQ ID NO:80)
DRGFYFN (SEQ ID NO:81)
RGFYFNK (SEQ ID NO:82)
GFYFNKP (SEQ ID NO:83)
FYFNKPT (SEQ ID NO:84)
YFNKPTG (SEQ ID NO:85)
FNKPTGY (SEQ ID NO:86)
NKPTGYG (SEQ ID NO:87)
KPTGYGS (SEQ ID NO:88)
PTGYGSS (SEQ ID NO:89)
TGYGSSS (SEQ ID NO:90)
GYGSSSR (SEQ ID NO:91)
YGSSSRR (SEQ ID NO:92)
GSSSRRA (SEQ ID NO:93)
SSSRRAP (SEQ ID NO:94)
SSRRAPQ (SEQ ID NO:95)

(those including at least four residues from, and preferably wholly within, the preferred 36-44 region, RRAPQTGIV) (SEQ ID NO:37)

SSSRRAP (SEQ ID NO:96)
SSRRAPQ (SEQ ID NO:97)
SRRAPQT (SEQ ID NO:98)
RRAPQTG (SEQ ID NO:99)
RAPQTGI (SEQ ID NO:100)
APQTGIV (SEQ ID NO:101)
PQTGIVD (SEQ ID NO:102)
QTGIVDE (SEQ ID NO:103)
TGIVDEC (SEQ ID NO:104)

(those including at least four residues from, and preferably wholly within, the 45-53 region, DECCFRSCD) (SEQ ID NO:46)
GIVDECC (SEQ ID NO:105)
IVDECCF (SEQ ID NO:106)
VDECCFR (SEQ ID NO:107)
DECCFRS (SEQ ID NO:108)
ECCFRSC (SEQ ID NO:109)
CCFRSCD (SEQ ID NO:110)
CFRSCDL (SEQ ID NO:111)
FRSCDLR (SEQ ID NO:112)
RSCDLRR (SEQ ID NO:113)

(those including at least four residues from, and preferably wholly within, the 54-60 region, LRRLEMY) (SEQ ID NO:55)
SCDLRRL (SEQ ID NO:114)
CDLRRLE (SEQ ID NO:115)
DLRRLEM (SEQ ID NO:116)
LRRLEMY (SEQ ID NO:117)
RRLEMYC (SEQ ID NO:118)
RLEMYCA (SEQ ID NO:119)
LEMYCAP (SEQ ID NO:120)

Octameric peptides derived from the regions of IGF-I identified as preferred include:

(those including at least four residues from, and preferably wholly within, the 1-17 region, GPETLCGAELVDALQFV) (SEQ ID NO: 2)
GPETLCGA (SEQ ID NO:121)
PETLCGAE (SEQ ID NO:122)
ETLCGAEL (SEQ ID NO:123)
TLCGAELV (SEQ ID NO:124)
LCGAELVD (SEQ ID NO:125)
CGAELVDA (SEQ ID NO:126)
GAELVDAL (SEQ ID NO:127)
AELVDALQ (SEQ ID NO:128)
ELVDALQF (SEQ ID NO:129)
LVDALQFV (SEQ ID NO:130)
VDALQFVC (SEQ ID NO:131)

DALQFVCG (SEQ ID NO:132)
ALQFVCGD (SEQ ID NO:133)
LQFVCGDR (SEQ ID NO:134)

(encompassing the 18-21 region, CGDR) (SEQ ID NO:17)
LQFVCGDR (SEQ ID NO:134)
QFVCGDRG (SEQ ID NO:135)
FVCGDRGF (SEQ ID NO:136)
VCGDRGFY (SEQ ID NO:137)
CGDRGFYF (SEQ ID NO:138)

(those including at least four residues from, and preferably wholly within, the 22-37 region, GFYFNKPTGYGSSSRR) (SEQ ID NO:21)
CGDRGFYF (SEQ ID NO:138)
GDRGFYFN (SEQ ID NO:139)
DRGFYFNK (SEQ ID NO:140)
RGFYFNKP (SEQ ID NO:141)
GFYFNKPT (SEQ ID NO:142)
FYFNKPTG (SEQ ID NO:143)
YFNKPTGY (SEQ ID NO:144)
FNKPTGYG (SEQ ID NO:145)
NKPTGYGS (SEQ ID NO:146)
KPTGYGSS (SEQ ID NO:147)
PTGYGSSS (SEQ ID NO:148)
TGYGSSSR (SEQ ID NO:149)
GYGSSSRR (SEQ ID NO:150)
YGSSSRRA (SEQ ID NO:151)
GSSSRRAP (SEQ ID NO:152)
SSSRRAPQ (SEQ ID NO:153)
SSRRAPQT (SEQ ID NO:154)

(those including at least four residues from, and preferably wholly within, the preferred 36-44 region, RRAPQTGIV) (SEQ ID NO:37)

GSSSRRAP (SEQ ID NO:152)
SSSRRAPQ (SEQ ID NO:153)
SSRRAPQT (SEQ ID NO:154)
SRRAPQTG (SEQ ID NO:155)
RRAPQTGI (SEQ ID NO:156)
RAPQTGIV (SEQ ID NO:157)
APQTGIVD (SEQ ID NO:158)
PQTGIVDE (SEQ ID NO:159)
QTGIVDEC (SEQ ID NO:160)
TGIVDECC (SEQ ID NO:161)

(those including at least four residues from, and preferably wholly within, the 45-53 region, DECCFRSCD) (SEQ ID NO:46)

TGIVDECC (SEQ ID NO:161)

GIVDECCF (SEQ ID NO:162)
IVDECCFR (SEQ ID NO:163)
VDECCFRS (SEQ ID NO:164)
DECCFRSC (SEQ ID NO:165)
ECCFRSCD (SEQ ID NO:166)
CCFRSCDL (SEQ ID NO:167)
CFRSCDLR (SEQ ID NO:168)
FRSCDLRR (SEQ ID NO:169)
RSCDLRRL (SEQ ID NO:170)

(those including at least four residues from, and preferably the whole of, the 54-60 region, LRRLEMY) (SEQ ID NO:55)
RSCDLRRL (SEQ ID NO:170)
SCDLRRLE (SEQ ID NO:171)
CDLRRLEM (SEQ ID NO:172)
DLRRLEMY (SEQ ID NO:173)
LRRLEMYC (SEQ ID NO:174)
RRLEMYCA (SEQ ID NO:175)
RLEMYCAP (SEQ ID NO:176)
LEMYCAPL (SEQ ID NO:177)

Both specific binding molecules and antigenic molecules in accordance with the invention will usually be intended to be administered parenterally, whether by injection, infusion or implantation. They will therefore generally be formulated as sterile preparations with a suitable carrier (such as water for injections or phosphate-buffered saline). Antigenic molecules within the invention may be formulated with a suitable adjuvant (such as alhydrogel) to boost antigenicity.

The invention may be used to enhance the activity of IGF-I, whether endogenous in the subject or exogenously administered. Formulations of specific binding molecules, or antigenic molecules, in accordance with the invention and IGF-I itself are therefore contemplated. Further, the specific binding molecules or antigenic molecules of the invention may be administered separat ly, simultaneously or sequentially with IGF-I.

The inv ntion is useful in a method of treating or preventing conditions in which IGF-I is useful, particularly those mentioned earlier. The invention therefore relates to the use of molecules in accordance with the invention in the manufacture of a medicament for treating or preventing conditions in which IGF-I is useful.

The invention will now be illustrated by the following examples. The examples refer to the accompanying drawings, in which:

FIGURE 1a shows the binding of anti-IGF-I antiserum to IGF-I;

FIGURE 1b shows the binding of anti-IGF-I antiserum to IGF-I peptide 1-17;

FIGURE 1c shows the results of peptide scanning to identify certain IGF-I binding regions recognised by anti-IGF-I antiserum;

FIGURE 2 shows the effect of anti-IGF-I antiserum on whole body weight gain in dwarf mice;

FIGURE 3 shows the effect of anti-IGF-I antiserum on liver weight gain in dwarf mice;

FIGURE 4 shows the effect of anti-IGF-I antiserum on whole body weight gain in dwarf rats;

FIGURE 5 shows the effect of anti-IGF-I antiserum on gastrocnemius muscle weight in dwarf rats;

FIGURE 6 shows the effect of semi-purified anti-IGF-I immunoglobulin on whole body weight gain in dwarf rats; and

FIGURE 7 shows the effect of semi-purified anti-IGF-I immunoglobulin on total leg muscle (gastrocnemius, plantaris and soleus) weight in dwarf rats.

Antibody Production

Polyclonal antibodies were raised against recombinant human IGF-I using adult wether Poll Dorset sheep. IGF-I was conjugated to human α-globulin using glutaraldehyde as follows: IGF-I (2 mg) was dissolved in 1.2 ml phosphate buffered saline (PBS, 100 mM sodium phosphate, pH 7.2). Human α-globulin (0.4 ml of a 5 mg/ml solution in PBS) and glutaraldehyde (0.4 ml of 0.4% grade I glutaraldehyde solution in water) were added and the conjugation allowed to proceed at room temperature for 20 min at which point 1.2 ml PBS were added. The mixture was immediately mixed with 6.4 ml Freund's adjuvant (complete for the prime immunisation and incomplete for subsequent boosts) using a POLYTRON homogeniser. (The word POLYTRON is a trade mark.) 2 ml were injected into sheep immediately (as 2 x 0.5 ml subcutaneously and 2 x 0.5 ml intramuscularly). The sheep were challenged every two months for a period of one year.

The titre of the antiserum was determined using standard ELISA techniques. ELISA plates (96 well) were coated for 1 h at 37°C and overnight at 4°C with a 2 μg/ml solution of IGF-I in carbonate buffer (100 mM sodium carbonate, pH 9.6). The plates were then rinsed three times with PBS containing 0.1% Tween 20 and blocked for 2 h at 37°C with 0.5% bovine serum albumin (BSA) in PBS. The wells

were emptied of blocking r agent and antis rum (100 µl of appropriate dilutions in PBS containing 0.1% Tween-20 and 0.5% BSA was added. The plates were incubated for 1 h at 37°C and were then washed three times using PBS containing 0.1% Tween-20. Biotinylated anti-sheep immunoglobulin (commercial preparation from Amersham International plc, Amersham, UK) was added (100 µl of a 1:1000 dilution in the PBS/Tween-20/BSA buffer) and incubated for 1 h at 37°C, after which time the plates were washed three times in PBS/Tween-20 buffer. Subsequently, streptavidin biotin horseradish peroxidase (100 µl of a 1:1000 dilution in PBS/Tween 20/BSA) was added and incubated at 37°C for 1 h followed by washing three times in PBS/Tween-20 buffer. Substrate reagent was then added (100 µl of 0.55 mg/ml 2,2'-azino-*bis*(3-ethylbenzthiazoline-6-sulphonic acid, diammonium salt in 100 mM citrate buffered saline, pH 4.3 containing 1.2 µl 30% hydrogen peroxide per 20 ml). The optical density of the wells was measured at a wavelength of 405 nm at appropriate time intervals (5 to 20 min after addition of substrate reagent).

The anti-IGF-I antiserum was prepared by taking blood from sheep 50, allowing the blood to clot at 4°C for 4 h, centrifuging at 2,500 g for 30 min and harvesting the supernatant serum. Titres for IGF-I of 1 in 5,000 (for 50% binding) were determined by ELISA (Figure 1a). The antibody binds to IGF-I in the region of residues 1-17 determined by ELISA as described above when peptide 1-17 was used to coat the plates in place of IGF-I (Figure 1b); the antibody could also bind to other epitopes on IGF-I. The antibody exhibited negligible binding to insulin or insulin-like growth factor-II.

Example 1: The effects of anti-IGF-I antiserum on growth in dwarf mice

Homozygous Snell dwarf mice have a genetic lesion resulting in almost negligible growth hormone, prolactin and thyroid stimulating hormone secretion by the pituitary gland and therefore almost negligible circulating IGF-I concentrations; tissue concentrations are unknown. The mice therefore provide a very sensitive model for the investigation of IGF-I activity. Homozygous dwarf mice were bred from a heterozygous colony at the Institute of Animal Physiology and Genetics Research and nine-week old mice (males and females) were randomly allocated to one of five treatment groups (n=6 per group):

Group	Treatment
1	Saline (0.15% sterile sodium chloride, 400 µl)
2	IGF-I (20 µg/d in 400 µl saline)
3	IGF-I (50 µg/d in 400 µl saline)
4	Anti-IGF-I antiserum (400 µl)
5	Anti-IGF-I antiserum (400 µl) pre-incubated for 1 h at room temperature with 20 µg/d IGF-I

Mice were given good quality pelleted rodent feed and water *ad libitum* and were housed as five animals per cage (one from each treatment group). Daily treatments were administered subcutaneously as two equal aliquots at 9am and 4pm for seven days, starting when the mice were ten weeks old. Whole body weight was recorded daily at 9am prior to injection and tissues were dissected out and weighed at slaughter (by decapitation). The data were analysed by one-way analysis of variance.

Figure 2 shows th whole body weight gain of the mic . Weight gain increased in a dose-dependent manner in response to IGF-I alone. Mice administered the anti-IGF-I antiserum in complex with 20 μg IGF-I per day exhibited at least a two-fold increase in daily gain compared with mice treated with 50 μg IGF-I alone ($P<0.001$). The data imply antiserum enhancement of IGF-I activity. Liver weights are illustrated in Figure 3. Injection of IGF-I alone did not change liver weight, whereas anti-IGF-I antiserum alone or in complex with IGF-I increased liver weight ($P<0.05$ and $P<0.01$, respectively) implying potentiation of endogenous and exogenous IGF-I action.

Example 2: The effects of anti-IGF-I antiserum on growth in dwarf rats

Homozygous dwarf rats have a genetic lesion resulting in low (but not negligible) GH secretion and therefore reduced circulating IGF-I concentrations (about 25% of normal levels), resulting in a chronically reduced growth rate. Female homozygous dwarf rats were bred from a colony at the Institute of Animal Physiology and Genetics Research and eight-week old dwarf rats were randomly allocated to one of four treatment groups (n=6 per group):

Group	Treatment
1	Non-immune serum (NIS, 3.0 ml/d)
2	Non-immune serum (3.0 ml/d) pre-incubated for 1 h at room temperature with 150 μg IGF-I/d
3	Anti-IGF-I antiserum (3.0 ml/d)
4	Anti-IGF-I antiserum (3.0 ml/d) pre-incubated for 1 h at room temperature with 150 μg IGF-I/d

Non-immune serum was prepared from blood derived from normal control wether sheep (Poll Dorset). Daily treatments were administered subcutaneously as two equal aliquots at 9am and 4pm for seven days when the rats were nine weeks old. Whole body and tissue weights were recorded and the data analysed by two-way analysis of variance with IGF-I and antiserum as main treatment effects.

Figure 4 shows the whole-body weight gain of the rats. Rats treated with anti-IGF-I antiserum (anti-IGF-I) grew faster than those treated with non-immune serum. Daily gains (g/d) are summarised below:

NIS	NIS +IGF	Anti-IGF-I	Anti-IGF +IGF	S.E.D. (n=6)	Main effects IGF	Anti-IGF-I
0.16	0.47	0.64	1.23	0.38	NS	0.032

IGF-I alone did not induce a significant increase in average daily gain whereas treatment with test antiserum did (P=0.032). The data imply that antiserum to IGF-I can enhance both endogenous and exogenous IGF-I.

Figure 5 shows the muscle weights (gastrocnemius) dissected out at slaughter. No statistically significant changes were observed but the IGF-I antiserum complex tended to induce increased muscle weight.

Example 3: The effects of semi-purified anti-IGF-I immunoglobulin on growth in dwarf rats

Semi-purified immunoglobulin was prepared from non-immune and anti-IGF-I antiserum by incubating the serum with saturated ammonium sulphate (0.666 x original serum volume) for 10 min at room temperature. The resultant

precipitate was isolated by centrifugation at 10,000 g at 4°C for 10 min. The pellet was resuspended in distilled water to the original serum volume and re-mixed with fresh saturated ammonium sulphate (0.666 x serum volume). The immunoglobulin was isolated by centrifugation as before and the pellet resuspended in a minimum volume of PBS and dialysed extensively against PBS to remove ammonium sulphate. The immunoglobulin solution was then diluted to half of the original serum volume. The anti-IGF-I immunoglobulin preparation had a titre for IGF-I of approximately double that of the original serum when equivalent volumes were tested and the non-immune serum exhibited negligible IGF-I binding as determined by the ELISA assay.

Eight-week old female homozygous dwarf rats (as in Example 2) were allocated to one of four treatment groups:

Group	Treatment
1	Semi-purified non-immune immunoglobulin (1.5 ml/d)
2	Semi-purified non-immune immunoglobulin (1.5 ml/d) pre-incubated for 1 h at room temperature with 150 µg IGF-I/d
3	Semi-purified anti-IGF-I immunoglobulin (1.5 ml/d)
4	Semi-purified anti-IGF-I immunoglobulin (1.5 ml/d) pre-incubated for 1 h at room temperature with 150 µg IGF-I/d

Daily treatments were administered subcutaneously as two qual aliquots at 9am and 4pm for ten days when the rats were nine weeks old. Whole body and tissue w ights were

recorded and the data analysed by two-way analysis of variance with IGF-I and antiserum as main treatment effects.

Whole body weight gains are illustrated in Figure 6. Average daily gains were calculated for each group as g/d and are presented below. When main effects of IGF-I and antiserum were considered, IGF-I induced no significant growth stimulation, whereas anti-IGF-I immunoglobulin did (P=0.035). These data imply enhancement of exogenous and endogenous IGF-I activity.

The total weights of dissected leg muscles (gastrocnemius, plantaris, soleus) are presented in Figure 7. As main effects, both IGF-I (P=0.010) and anti-IGF-I antiserum (P=0.018) stimulated significant increases in muscle weight. These total changes were reflected in the individual muscle weights, given below.

	NIS	NIS +IGF	Anti-IGF-I	Anti-IGF +IGF	S.E.D. (n=6)	Main effects: IGF	Anti-IGF-I
Whole body daily gain (g/d)	0.47	0.51	0.86	1.35	0.38	NS	0.035
Gastrocnemius weight (g)	1.508	1.557	1.532	1.687	0.045	0.005	0.026
Plantaris weight (g)	0.285	0.280	0.295	0.303	0.010	NS	0.044
Soleus weight (g)	0.113	0.118	0.117	0.124	0.006	NS	NS

Example 4 - Peptide scanning

This example shows the results of peptide scanning the enhancing polyclonal anti-IGF-I antibody from sheep 50 (see "Antibody Production", immediately before Example 1). Th protocol used 6mers and 8mers along the IGF-I sequence and identified the following residues as possible enhancing epitopes: 11-17, 18-21, 36-44 (very

strong), 45-53 and 54-60. These are illustrated in Figure 1c. The methodology used was exactly as described in the manufacturer's instructions (Cambridge Research Biochemicals, Northwich, Cheshire: Epitope Scanning Kit).

Example 5 - Effects of antibodies to specific peptide regions of IGF-I

Antibodies raised in sheep to the following peptide regions have enhanced IGF-I activity, at least in terms of weight gain in dwarf rats: 1-17, 22-37, 59-70; antibodies raised to peptide 49-58 appear to have inhibited this particular IGF-I action. The method followed was as: Lachmann, P.J., Strangeways, L., Vyakarnam, A & Evan, G.I. (1986) "Raising antibodies by coupling peptides to PPD and immunizing BCG-sensitized animals", In Synthetic Peptides as Antigens, Ciba Foundation Symposium, 119, pp 25-40. John Wiley & Sons: London and New York. (PPD=purified protein derivative of tuberculin and BCG=Bacillus Calmette-Guerin). The methodology used for the animal experiment is exactly as for Example 3 except 200 μg IGF-I per day were used, not 150 μg/day, and the experiment was for 7 days and analysis was by one-way analysis of variance. Treatment groups and weight gain at 7 days was as follows:

Group	Treatment	Whole body wt. gain at 7 d (g)
Control	Semi-purified non-immune immunoglobulin (1.5 ml/day)	5.43
IGF-I	Semi-purified non-immune immunoglobulin (1.5 ml/day) pre-incubated for 1 h at room temperature with 200 µg IGF-I/day	7.30
IGF-I plus anti-1-17	Semi-purified anti-1-17 immunoglobulin (1.5 ml/day) pre-incubated for 1 h at room temperature with 200 µg IGF-I/day	11.34*
IGF-I plus anti-49-58	Semi-purified anti-49-58 immunoglobulin (1.5 ml/day) pre-incubated for 1 h at room temperature with 200 µg IGF-I/day	4.83
IGF-I plus anti-22-37	Semi-purified anti-22-37 immunoglobulin (1.5 ml/day) pre-incubated for 1 h at room temperature with 200 µg IGF-I/day	11.16*
IGF-I plus anti-59-70	Semi-purified anti-59-70 immunoglobulin (1.5 ml/day) pre-incubated for 1 h at room temperature with 200 µg IGF-I/day	9.54
S.E.D. (n=7)		0.1675

* sig. diff from IGF-I plus non-immune immunoglobulin ($P<0.05$)

Example 6: Synthesis of Predicted Enhancing Epitopes and Production of Antibodies to these Peptide Sequences

Peptide synthesis

The region of IGF-I which showed very strong binding to the enhancing anti-IGF-I antiserum was synthesised as two peptides using a Millipore/Biosearch 9500 peptide synthesiser (New Brunswick Scientific UK Ltd, Watford, England). The peptides were:

APQTGIVDC (SEQ ID NO:158)

PQTGIVDEC (SEQ ID NO:159)

The C residues were added for conjugation purposes.

Peptide conjugation

The peptides were conjugated via the C residue to purified protein derivative of tuberculin (PPD, from Statens Seruminstitute, Copenhagen, Denmark) using sulphosuccinimidyl 4-(N-maleimidomethyl)-cyclohexane-1-carboxylate (sulpho-SMCC, Pierce Chemical Company, Rockford, USA). PPD elicits its own delayed hypersensitivity reaction in animals which have encountered tubercle bacillus. A 10 ml vial of PPD (1 mg/ml) was freeze-dried overnight and reconstituted with 2 ml glass distilled water. 2.5 mg sulpho-SMCC were added and the solids dissolved using an ultrasonic water bath. The pH of the solution was adjusted to 7.5 with 4 M NaOH and incubated at room temperature for 30 min. The solution was added to a 1.6 cm x 22 cm Ultrogel AcA 202 gel filtration column (IBF Biotechnics, Villeneuve-la-Garenne, France) and eluted at 4°C with 50 mM sodium phosphate buffer, pH 6.0. Activated PPD emerged at the exclusion volume of the column and unreacted sulpho-SMCC in later fractions; 10 mg peptide was pooled with activated PPD. After adjusting the pH to 7.0 with 5 M NaOH the solution was gassed with nitrogen and stored at room temperature overnight. The volume was adjusted to 10 ml using distilled water and stored at -70°C in 1 ml aliquots.

Production of antibodies in sheep

Four sheep (Poll Dorset wethers aged one year) were injected with Bacillus Calmette-Guérin (BCG, reconstituted from freeze dried material with distilled water) as a 0.1 ml intradermal injection (equivalent to 8×10^5 colony forming units).

One month after the BCG injections, 1 ml conjugated peptide was homogenised with 3 ml Freund's Incomplete Adjuvant and the sheep were injected with two by 0.75 ml emulsion intramuscularly plus two by 0.25 ml injections subcutaneously. Two sheep were immunised with each of the two peptides specified above. Boosts were carried out at 3 week intervals as described here except two by 0.5 ml injections were given intramuscularly and two by 0.5 ml injections subcutaneously. Serum was collected 10 days after each boost for antibody purification.

SEQUENCE LISTING

(1) GENERAL INFORMATION:

(i) APPLICANT:
(A) NAME: THE AGRCULTURAL AND FOOD RESEARCH COUNCIL
(B) STREET: BABRAHAM HALL
(C) CITY: CAMBRIDGE
(E) COUNTRY: GREAT BRITAIN
(F) POSTAL CODE (ZIP): CB2 4AT

(ii) TITLE OF INVENTION: ANTIBODY-MEDIATED ENHANCEMENT OF IGF-I ACTIVITY

(iii) NUMBER OF SEQUENCES: 1

(iv) COMPUTER READABLE FORM:
(A) MEDIUM TYPE: Floppy disk
(B) COMPUTER: IBM PC compatible
(C) OPERATING SYSTEM: PC-DOS/MS-DOS
(D) SOFTWARE: PatentIn Release #1.0, Version #1.25 (EPO)

(2) INFORMATION FOR SEQ ID NO: 1:

(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 70 amino acids
(B) TYPE: amino acid
(D) TOPOLOGY: linear

(ii) MOLECULE TYPE: peptide

(v) FRAGMENT TYPE: N-terminal

(ix) FEATURE:
(A) NAME/KEY: Peptide
(B) LOCATION: 1..70
(D) OTHER INFORMATION: /note= "1-70 REGION OF HUMAN IGF-I"

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 1:

Gly Pro Glu Thr Leu Cys Gly Ala Glu Leu Val Asp Ala Leu Gln Phe
1 5 10 15

Val Cys Gly Asp Arg Gly Phe Tyr Phe Asn Lys Pro Thr Gly Tyr Gly
20 25 30

Ser Ser Ser Arg Arg Ala Pro Gln Thr Gly Ile Val Asp Glu Cys Cys
35 40 45

Phe Arg Ser Cys Asp Leu Arg Arg Leu Glu Met Tyr Cys Ala Pro Leu
50 55 60

Lys Pro Ala Lys Ser Ala
65 70

(2) INFORMATION FOR SEQ ID NO: 2:

(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 17 amino acids
(B) TYPE: amino acid
(D) TOPOLOGY: linear

(ii) MOLECULE TYPE: peptide

(v) FRAGMENT TYPE: N-terminal

(ix) FEATURE:
(A) NAME/KEY: Peptide
(B) LOCATION: 1..17
(D) OTHER INFORMATION: /note= "1-17 REGION OF HUMAN IGF-I"

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 2:

Gly Pro Glu Thr Leu Cys Gly Ala Glu Leu Val Asp Ala Leu Gln Phe
1 5 10 15

Val
17

(2) INFORMATION FOR SEQ ID NO: 3:

(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 6 amino acids
(B) TYPE: amino acid
(D) TOPOLOGY: linear

(ii) MOLECULE TYPE: peptide

(v) FRAGMENT TYPE: N-terminal

(ix) FEATURE:
(A) NAME/KEY: Peptide
(B) LOCATION: 1..6
(D) OTHER INFORMATION: /note= "1-6 REGION OF HUMAN IGF-I"

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 3:

Gly Pro Glu Thr Leu Cys
1 5

(2) INFORMATION FOR SEQ ID NO: 4:

(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 6 amino acids
(B) TYPE: amino acid
(D) TOPOLOGY: linear

(ii) MOLECULE TYPE: peptide

(v) FRAGMENT TYPE: internal

(ix) FEATURE:
(A) NAME/KEY: Peptide
(B) LOCATION: 1..6
(D) OTHER INFORMATION: /note= "2-7 REGION OF HUMAN IGF-I"

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 4:

Pro Glu Thr Leu Cys Gly
1 5

(2) INFORMATION FOR SEQ ID NO: 5:

(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 6 amino acids
(B) TYPE: amino acid
(D) TOPOLOGY: linear

(ii) MOLECULE TYPE: peptide

(v) FRAGMENT TYPE: internal

(ix) FEATURE:
(A) NAME/KEY: Peptide
(B) LOCATION: 1..6
(D) OTHER INFORMATION: /note= "3-8 REGION OF HUMAN IGF-I"

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 5:

Glu Thr Leu Cys Gly Ala
1 5

(2) INFORMATION FOR SEQ ID NO: 6:

(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 6 amino acids
(B) TYPE: amino acid
(D) TOPOLOGY: linear

(ii) MOLECULE TYPE: peptide

(v) FRAGMENT TYPE: internal

(ix) FEATURE:
(A) NAME/KEY: Peptide
(B) LOCATION: 1..6
(D) OTHER INFORMATION: /note= "4-9 REGION OF HUMAN IGF-I"

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 6:

Thr Leu Cys Gly Ala Glu
1 5

(2) INFORMATION FOR SEQ ID NO: 7:

(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 6 amino acids
(B) TYPE: amino acid
(D) TOPOLOGY: linear

(ii) MOLECULE TYPE: peptide

(v) FRAGMENT TYPE: internal

(ix) FEATURE:
(A) NAME/KEY: Peptide
(B) LOCATION: 1..6
(D) OTHER INFORMATION: /note= "5-10 REGION OF HUMAN IGF-I"

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 7:

Leu Cys Gly Ala Glu Leu
1 5

(2) INFORMATION FOR SEQ ID NO: 8:

(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 6 amino acids
(B) TYPE: amino acid
(D) TOPOLOGY: linear

(ii) MOLECULE TYPE: peptide

(v) FRAGMENT TYPE: internal

(ix) FEATURE:
(A) NAME/KEY: Peptide
(B) LOCATION: 1..6
(D) OTHER INFORMATION: /note= "6-11 REGION OF HUMAN IGF-I"

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 8:

Cys Gly Ala Glu Leu Val
1 5

(2) INFORMATION FOR SEQ ID NO: 9:

(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 6 amino acids
(B) TYPE: amino acid
(D) TOPOLOGY: linear

(ii) MOLECULE TYPE: peptide

(v) FRAGMENT TYPE: internal

(ix) FEATURE:
(A) NAME/KEY: Peptide
(B) LOCATION: 1..6
(D) OTHER INFORMATION: /note= "7-12 REGION OF HUMAN IGF-I"

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 9:

Gly Ala Glu Leu Val Asp
1 5

(2) INFORMATION FOR SEQ ID NO: 10:

(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 6 amino acids
(B) TYPE: amino acid
(D) TOPOLOGY: linear

(ii) MOLECULE TYPE: peptide

(v) FRAGMENT TYPE: internal

(ix) FEATURE:
(A) NAME/KEY: Peptide
(B) LOCATION: 1..6
(D) OTHER INFORMATION: /note= "8-13 REGION OF HUMAN IGF-I"

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 10:

Ala Glu Leu Val Asp Ala
1 5

(2) INFORMATION FOR SEQ ID NO: 11:

(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 6 amino acids
(B) TYPE: amino acid
(D) TOPOLOGY: linear

(ii) MOLECULE TYPE: peptide

(v) FRAGMENT TYPE: internal

(ix) FEATURE:
(A) NAME/KEY: Peptide
(B) LOCATION: 1..6
(D) OTHER INFORMATION: /note= "9-14 REGION OF HUMAN IGF-I"

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 11:

Glu Leu Val Asp Ala Leu
1 5

(2) INFORMATION FOR SEQ ID NO: 12:

(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 6 amino acids
(B) TYPE: amino acid
(D) TOPOLOGY: linear

(ii) MOLECULE TYPE: peptide

(v) FRAGMENT TYPE: internal

(ix) FEATURE:
(A) NAME/KEY: Peptide
(B) LOCATION: 1..6
(D) OTHER INFORMATION: /note= "10-15 REGION OF HUMAN IGF-I"

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 12:

Leu Val Asp Ala Leu Gln
1 5

(2) INFORMATION FOR SEQ ID NO: 13:

(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 6 amino acids
(B) TYPE: amino acid
(D) TOPOLOGY: linear

(ii) MOLECULE TYPE: peptide

(v) FRAGMENT TYPE: internal

(ix) FEATURE:
(A) NAME/KEY: Peptide
(B) LOCATION: 1..6
(D) OTHER INFORMATION: /note= "11-16 REGION OF HUMAN IGF-I"

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 13:

Val Asp Ala Leu Gln Phe
1 5

(2) INFORMATION FOR SEQ ID NO: 14:

(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 6 amino acids
(B) TYPE: amino acid
(D) TOPOLOGY: linear

(ii) MOLECULE TYPE: peptide

(v) FRAGMENT TYPE: internal

(ix) FEATURE:
(A) NAME/KEY: Peptide
(B) LOCATION: 1..6
(D) OTHER INFORMATION: /note= "12-17 REGION OF HUMAN IGF-I"

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 14:

Asp Ala Leu Gln Phe Val
1 5

(2) INFORMATION FOR SEQ ID NO: 15:

(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 6 amino acids
(B) TYPE: amino acid
(D) TOPOLOGY: linear

(ii) MOLECULE TYPE: peptide

(v) FRAGMENT TYPE: internal

(ix) FEATURE:
(A) NAME/KEY: Peptide
(B) LOCATION: 1..6
(D) OTHER INFORMATION: /note= "13-18 REGION OF HUMAN IGF-I"

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 15:

Ala Leu Gln Phe Val Cys
1 5

(2) INFORMATION FOR SEQ ID NO: 16:

(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 6 amino acids
(B) TYPE: amino acid
(D) TOPOLOGY: linear

(ii) MOLECULE TYPE: peptide

(v) FRAGMENT TYPE: internal

(ix) FEATURE:
(A) NAME/KEY: Peptide
(B) LOCATION: 1..6
(D) OTHER INFORMATION: /note= "14-19 REGION OF HUMAN IGF-I"

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 16:

Leu Gln Phe Val Cys Gly
1 5

(2) INFORMATION FOR SEQ ID NO: 17:

(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 4 amino acids
(B) TYPE: amino acid
(D) TOPOLOGY: linear

(ii) MOLECULE TYPE: peptide

(v) FRAGMENT TYPE: internal

(ix) FEATURE:
(A) NAME/KEY: Peptide
(B) LOCATION: 1..4
(D) OTHER INFORMATION: /note= "18-21 REGION OF HUMAN IGF-I"

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 17:

Cys Gly Asp Arg
1

(2) INFORMATION FOR SEQ ID NO: 18:

(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 6 amino acids
(B) TYPE: amino acid
(D) TOPOLOGY: linear

(ii) MOLECULE TYPE: peptide

(v) FRAGMENT TYPE: internal

(ix) FEATURE:
(A) NAME/KEY: Peptide
(B) LOCATION: 1..6
(D) OTHER INFORMATION: /note= "16-21 REGION OF HUMAN IGF-I"

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 18:

Phe Val Cys Gly Asp Arg
1 5

(2) INFORMATION FOR SEQ ID NO: 19:

(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 6 amino acids
(B) TYPE: amino acid
(D) TOPOLOGY: linear

(ii) MOLECULE TYPE: peptide

(v) FRAGMENT TYPE: internal

(ix) FEATURE:
(A) NAME/KEY: Peptide
(B) LOCATION: 1..6
(D) OTHER INFORMATION: /note= "17-22 REGION OF HUMAN IGF-I"

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 19:

Val Cys Gly Asp Arg Gly
1 5

(2) INFORMATION FOR SEQ ID NO: 20:

(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 6 amino acids
(B) TYPE: amino acid
(D) TOPOLOGY: linear

(ii) MOLECULE TYPE: peptide

(v) FRAGMENT TYPE: internal

(ix) FEATURE:
(A) NAME/KEY: Peptide
(B) LOCATION: 1..6
(D) OTHER INFORMATION: /note= "18-23 REGION OF HUMAN IGF-I"

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 20:

Cys Gly Asp Arg Gly Phe
1 5

(2) INFORMATION FOR SEQ ID NO: 21:

(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 16 amino acids
(B) TYPE: amino acid
(D) TOPOLOGY: linear

(ii) MOLECULE TYPE: peptide

(v) FRAGMENT TYPE: internal

(ix) FEATURE:
(A) NAME/KEY: Peptide
(B) LOCATION: 1..16
(D) OTHER INFORMATION: /note= "22-37 REGION OF HUMAN IGF-I"

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 21:

Gly Phe Tyr Phe Asn Lys Pro Thr Gly Tyr Gly Ser Ser Ser Arg Arg
1 5 10 15

(2) INFORMATION FOR SEQ ID NO: 22:

(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 6 amino acids
(B) TYPE: amino acid
(D) TOPOLOGY: linear

(ii) MOLECULE TYPE: peptide

(v) FRAGMENT TYPE: internal

(ix) FEATURE:
(A) NAME/KEY: Peptide
(B) LOCATION: 1..6
(D) OTHER INFORMATION: /note= "20-25 REGION OF HUMAN IGF-I"

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 22:

Asp Arg Gly Phe Tyr Phe
1 5

(2) INFORMATION FOR SEQ ID NO: 23:

(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 6 amino acids
(B) TYPE: amino acid
(D) TOPOLOGY: linear

(ii) MOLECULE TYPE: peptide

(v) FRAGMENT TYPE: internal

(ix) FEATURE:
(A) NAME/KEY: Peptide
(B) LOCATION: 1..6
(D) OTHER INFORMATION: /note= "21-26 REGION OF HUMAN IGF-I"

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 23:

Arg Gly Phe Tyr Phe Asn
1 5

(2) INFORMATION FOR SEQ ID NO: 24:

(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 6 amino acids
(B) TYPE: amino acid
(D) TOPOLOGY: linear

(ii) MOLECULE TYPE: peptide

(v) FRAGMENT TYPE: internal

(ix) FEATURE:
(A) NAME/KEY: Peptide
(B) LOCATION: 1..6
(D) OTHER INFORMATION: /note= "22-27 REGION OF HUMAN IGF-I"

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 24:

Gly Phe Tyr Phe Asn Lys
1 5

(2) INFORMATION FOR SEQ ID NO: 25:

(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 6 amino acids
(B) TYPE: amino acid
(D) TOPOLOGY: linear

(ii) MOLECULE TYPE: peptide

(v) FRAGMENT TYPE: internal

(ix) FEATURE:
(A) NAME/KEY: Peptide
(B) LOCATION: 1..6
(D) OTHER INFORMATION: /note= "23-28 REGION OF HUMAN IGF-I"

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 25:

Phe Tyr Phe Asn Lys Pro
1 5

(2) INFORMATION FOR SEQ ID NO: 26:

(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 6 amino acids
(B) TYPE: amino acid
(D) TOPOLOGY: linear

(ii) MOLECULE TYPE: peptide

(v) FRAGMENT TYPE: internal

(ix) FEATURE:
(A) NAME/KEY: Peptide
(B) LOCATION: 1..6
(D) OTHER INFORMATION: /note= "24-29 REGION OF HUMAN IGF-I"

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 26:

Tyr Phe Asn Lys Pro Thr
1 5

(2) INFORMATION FOR SEQ ID NO: 27:

(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 6 amino acids
(B) TYPE: amino acid
(D) TOPOLOGY: linear

(ii) MOLECULE TYPE: peptide

(v) FRAGMENT TYPE: internal

(ix) FEATURE:
(A) NAME/KEY: Peptide
(B) LOCATION: 1..6
(D) OTHER INFORMATION: /note= "25-30 REGION OF HUMAN IGF-I"

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 27:

Phe Asn Lys Pro Thr Gly
1 5

(2) INFORMATION FOR SEQ ID NO: 28:

(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 6 amino acids
(B) TYPE: amino acid
(D) TOPOLOGY: linear

(ii) MOLECULE TYPE: peptide

(v) FRAGMENT TYPE: internal

(ix) FEATURE:
(A) NAME/KEY: Peptide
(B) LOCATION: 1..6
(D) OTHER INFORMATION: /note= "26-31 REGION OF HUMAN IGF-I"

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 28:

Asn Lys Pro Thr Gly Tyr
1 5

(2) INFORMATION FOR SEQ ID NO: 29:

(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 6 amino acids
(B) TYPE: amino acid
(D) TOPOLOGY: linear

(ii) MOLECULE TYPE: peptide

(v) FRAGMENT TYPE: internal

(ix) FEATURE:
(A) NAME/KEY: Peptide
(B) LOCATION: 1..6
(D) OTHER INFORMATION: /not = "27-32 REGION OF HUMAN IGF-I"

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 29:

Lys Pro Thr Gly Tyr Gly
1 5

(2) INFORMATION FOR SEQ ID NO: 30:

(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 6 amino acids
(B) TYPE: amino acid
(D) TOPOLOGY: linear

(ii) MOLECULE TYPE: peptide

(v) FRAGMENT TYPE: internal

(ix) FEATURE:
(A) NAME/KEY: Peptide
(B) LOCATION: 1..6
(D) OTHER INFORMATION: /note= "28-33 REGION OF HUMAN IGF-I"

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 30:

Pro Thr Gly Tyr Gly Ser
1 5

(2) INFORMATION FOR SEQ ID NO: 31:

(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 6 amino acids
(B) TYPE: amino acid
(D) TOPOLOGY: linear

(ii) MOLECULE TYPE: peptide

(v) FRAGMENT TYPE: internal

(ix) FEATURE:
(A) NAME/KEY: Peptide
(B) LOCATION: 1..6
(D) OTHER INFORMATION: /note= "29-34 REGION OF HUMAN IGF-I"

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 31:

Thr Gly Tyr Gly Ser Ser
1 5

(2) INFORMATION FOR SEQ ID NO: 32:

(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 6 amino acids
(B) TYPE: amino acid
(D) TOPOLOGY: linear

(ii) MOLECULE TYPE: peptide

(v) FRAGMENT TYPE: internal

(ix) FEATURE:
(A) NAME/KEY: Peptide
(B) LOCATION: 1..6
(D) OTHER INFORMATION: /note= "30-35 REGION OF HUMAN IGF-I"

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 32:

Gly Tyr Gly Ser Ser Ser
1 5

(2) INFORMATION FOR SEQ ID NO: 33:

(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 6 amino acids
(B) TYPE: amino acid
(D) TOPOLOGY: linear

(ii) MOLECULE TYPE: peptide

(v) FRAGMENT TYPE: internal

(ix) FEATURE:
(A) NAME/KEY: Peptide
(B) LOCATION: 1..6
(D) OTHER INFORMATION: /note= "31-36 REGION OF HUMAN IGF-I"

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 33:

Tyr Gly Ser Ser Ser Arg
1 5

(2) INFORMATION FOR SEQ ID NO: 34:

(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 6 amino acids
(B) TYPE: amino acid
(D) TOPOLOGY: linear

(ii) MOLECULE TYPE: peptide

(v) FRAGMENT TYPE: internal

(ix) FEATURE:
(A) NAME/KEY: Peptide
(B) LOCATION: 1..6
(D) OTHER INFORMATION: /note= "32-37 REGION OF HUMAN IGF-I"

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 34:

Gly Ser Ser Ser Arg Arg
1 5

(2) INFORMATION FOR SEQ ID NO: 35:

(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 6 amino acids
(B) TYPE: amino acid
(D) TOPOLOGY: linear

(ii) MOLECULE TYPE: peptide

(v) FRAGMENT TYPE: internal

(ix) FEATURE:
(A) NAME/KEY: Peptide
(B) LOCATION: 1..6
(D) OTHER INFORMATION: /note= "33-38 REGION OF HUMAN IGF-I"

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 35:

Ser Ser Ser Arg Arg Ala
1 5

(2) INFORMATION FOR SEQ ID NO: 36:

(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 6 amino acids
(B) TYPE: amino acid
(D) TOPOLOGY: linear

(ii) MOLECULE TYPE: peptide

(v) FRAGMENT TYPE: internal

(ix) FEATURE:
(A) NAME/KEY: Peptide
(B) LOCATION: 1..6
(D) OTHER INFORMATION: /note= "34-39 REGION OF HUMAN IGF-I"

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 36:

Ser Ser Arg Arg Ala Pro
1 5

(2) INFORMATION FOR SEQ ID NO: 37:

(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 9 amino acids
(B) TYPE: amino acid
(D) TOPOLOGY: linear

(ii) MOLECULE TYPE: peptide

(v) FRAGMENT TYPE: internal

(ix) FEATURE:
(A) NAME/KEY: Peptide
(B) LOCATION: 1..9
(D) OTHER INFORMATION: /note= "36-44 REGION OF HUMAN IGF-I"

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 37:

Arg Arg Ala Pro Gln Thr Gly Ile Val
1 5

(2) INFORMATION FOR SEQ ID NO: 38:

(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 6 amino acids
(B) TYPE: amino acid
(D) TOPOLOGY: linear

(ii) MOLECULE TYPE: peptide

(v) FRAGMENT TYPE: internal

(ix) FEATURE:
(A) NAME/KEY: Peptide
(B) LOCATION: 1..6
(D) OTHER INFORMATION: /note= "34-39 REGION OF HUMAN IGF-I"

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 38:

Ser Ser Arg Arg Ala Pro
1 5

(2) INFORMATION FOR SEQ ID NO: 39:

(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 6 amino acids
(B) TYPE: amino acid
(D) TOPOLOGY: linear

(ii) MOLECULE TYPE: peptide

(v) FRAGMENT TYPE: internal

(ix) FEATURE:
(A) NAME/KEY: Peptide
(B) LOCATION: 1..6
(D) OTHER INFORMATION: /note= "35-40 REGION OF HUMAN IGF-I"

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 39:

Ser Arg Arg Ala Pro Gln
1 5

(2) INFORMATION FOR SEQ ID NO: 40:

(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 6 amino acids
(B) TYPE: amino acid
(D) TOPOLOGY: linear

(ii) MOLECULE TYPE: peptide

(v) FRAGMENT TYPE: internal

(ix) FEATURE:
(A) NAME/KEY: Peptide
(B) LOCATION: 1..6
(D) OTHER INFORMATION: /note= "36-41 REGION OF HUMAN IGF-I"

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 40:

Arg Arg Ala Pro Gln Thr
1 5

(2) INFORMATION FOR SEQ ID NO: 41:

(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 6 amino acids
(B) TYPE: amino acid
(D) TOPOLOGY: linear

(ii) MOLECULE TYPE: peptide

(v) FRAGMENT TYPE: internal

(ix) FEATURE:
(A) NAME/KEY: Peptide
(B) LOCATION: 1..6
(D) OTHER INFORMATION: /note= "37-42 REGION OF HUMAN IGF-I"

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 41:

Arg Ala Pro Gln Thr Gly
1 5

(2) INFORMATION FOR SEQ ID NO: 42:

(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 6 amino acids
(B) TYPE: amino acid
(D) TOPOLOGY: linear

(ii) MOLECULE TYPE: peptide

(v) FRAGMENT TYPE: internal

(ix) FEATURE:
(A) NAME/KEY: Peptide
(B) LOCATION: 1..6
(D) OTHER INFORMATION: /note= "38-43 REGION OF HUMAN IGF-I"

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 42:

Ala Pro Gln Thr Gly Ile
1 5

(2) INFORMATION FOR SEQ ID NO: 43:

(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 6 amino acids
(B) TYPE: amino acid
(D) TOPOLOGY: linear

(ii) MOLECULE TYPE: peptide

(v) FRAGMENT TYPE: internal

(ix) FEATURE:
(A) NAME/KEY: Peptide
(B) LOCATION: 1..6
(D) OTHER INFORMATION: /note= "39-44 REGION OF HUMAN IGF-I"

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 43:

Pro Gln Thr Gly Ile Val
1 5

(2) INFORMATION FOR SEQ ID NO: 44:

(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 6 amino acids
(B) TYPE: amino acid
(D) TOPOLOGY: linear

(ii) MOLECULE TYPE: peptide

(v) FRAGMENT TYPE: internal

(ix) FEATURE:
(A) NAME/KEY: Peptide
(B) LOCATION: 1..6
(D) OTHER INFORMATION: /note= "40-45 REGION OF HUMAN IGF-I"

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 44:

Gln Thr Gly Ile Val Asp
1 5

(2) INFORMATION FOR SEQ ID NO: 45:

(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 6 amino acids
(B) TYPE: amino acid
(D) TOPOLOGY: linear

(ii) MOLECULE TYPE: peptide

(v) FRAGMENT TYPE: internal

(ix) FEATURE:
(A) NAME/KEY: Peptide
(B) LOCATION: 1..6
(D) OTHER INFORMATION: /note= "41-46 REGION OF HUMAN IGF-I"

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 45:

Thr Gly Ile Val Asp Glu
1 5

(2) INFORMATION FOR SEQ ID NO: 46:

(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 9 amino acids
(B) TYPE: amino acid
(D) TOPOLOGY: linear

(ii) MOLECULE TYPE: peptide

(v) FRAGMENT TYPE: internal

(ix) FEATURE:
(A) NAME/KEY: Peptide
(B) LOCATION: 1..9
(D) OTHER INFORMATION: /note= "45-53 REGION OF HUMAN IGF-I"

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 46:

Asp Glu Cys Cys Phe Arg Ser Cys Asp
1 5

(2) INFORMATION FOR SEQ ID NO: 47:

(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 6 amino acids
(B) TYPE: amino acid
(D) TOPOLOGY: linear

(ii) MOLECULE TYPE: peptide

(v) FRAGMENT TYPE: internal

(ix) FEATURE:
(A) NAME/KEY: Peptide
(B) LOCATION: 1..6
(D) OTHER INFORMATION: /note= "43-48 REGION OF HUMAN IGF-I"

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 47:

Ile Val Asp Glu Cys Cys
1 5

(2) INFORMATION FOR SEQ ID NO: 48:

(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 6 amino acids
(B) TYPE: amino acid
(D) TOPOLOGY: linear

(ii) MOLECULE TYPE: peptide

(v) FRAGMENT TYPE: internal

(ix) FEATURE:
(A) NAME/KEY: Peptide
(B) LOCATION: 1..6
(D) OTHER INFORMATION: /note= "44-49 REGION OF HUMAN IGF-I"

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 48:

Val Asp Glu Cys Cys Phe
1 5

(2) INFORMATION FOR SEQ ID NO: 49:

(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 6 amino acids
(B) TYPE: amino acid
(D) TOPOLOGY: linear

(ii) MOLECULE TYPE: peptide

(v) FRAGMENT TYPE: internal

(ix) FEATURE:
(A) NAME/KEY: Peptide
(B) LOCATION: 1..6
(D) OTHER INFORMATION: /note= "45-50 REGION OF HUMAN IGF-I"

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 49:

Asp Glu Cys Cys Phe Arg
1 5

(2) INFORMATION FOR SEQ ID NO: 50:

(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 6 amino acids
(B) TYPE: amino acid
(D) TOPOLOGY: linear

(ii) MOLECULE TYPE: peptide

(v) FRAGMENT TYPE: internal

(ix) FEATURE:
(A) NAME/KEY: Peptide
(B) LOCATION: 1..6
(D) OTHER INFORMATION: /note= "46-51 REGION OF HUMAN IGF-I"

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 50:

Glu Cys Cys Phe Arg Ser
1 5

(2) INFORMATION FOR SEQ ID NO: 51:

(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 6 amino acids
(B) TYPE: amino acid
(D) TOPOLOGY: linear

(ii) MOLECULE TYPE: peptide

(v) FRAGMENT TYPE: internal

(ix) FEATURE:
(A) NAME/KEY: Peptide
(B) LOCATION: 1..6
(D) OTHER INFORMATION: /note= "47-52 REGION OF HUMAN IGF-I"

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 51:

Cys Cys Phe Arg Ser Cys
1 5

(2) INFORMATION FOR SEQ ID NO: 52:

(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 6 amino acids
(B) TYPE: amino acid
(D) TOPOLOGY: linear

(ii) MOLECULE TYPE: peptide

(v) FRAGMENT TYPE: internal

(ix) FEATURE:
(A) NAME/KEY: Peptide
(B) LOCATION: 1..6
(D) OTHER INFORMATION: /note= "48-53 REGION OF HUMAN IGF-I"

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 52:

Cys Phe Arg Ser Cys Asp
1 5

(2) INFORMATION FOR SEQ ID NO: 53:

(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 6 amino acids
(B) TYPE: amino acid
(D) TOPOLOGY: linear

(ii) MOLECULE TYPE: peptide

(v) FRAGMENT TYPE: internal

(ix) FEATURE:
(A) NAME/KEY: Peptide
(B) LOCATION: 1..6
(D) OTHER INFORMATION: /note= "49-54 REGION OF HUMAN IGF-I"

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 53:

Phe Arg Ser Cys Asp Leu
1 5

(2) INFORMATION FOR SEQ ID NO: 54:

(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 6 amino acids
(B) TYPE: amino acid
(D) TOPOLOGY: linear

(ii) MOLECULE TYPE: peptide

(v) FRAGMENT TYPE: internal

(ix) FEATURE:
(A) NAME/KEY: P ptide
(B) LOCATION: 1..6
(D) OTHER INFORMATION: /note= "50-55 REGION OF HUMAN IGF-I"

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 54:

Arg Ser Cys Asp Leu Arg
1 5

(2) INFORMATION FOR SEQ ID NO: 55:

(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 7 amino acids
(B) TYPE: amino acid
(D) TOPOLOGY: linear

(ii) MOLECULE TYPE: peptide

(v) FRAGMENT TYPE: internal

(ix) FEATURE:
(A) NAME/KEY: Peptide
(B) LOCATION: 1..7
(D) OTHER INFORMATION: /note= "54-60 REGION OF HUMAN IGF-I"

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 55:

Leu Arg Arg Leu Glu Met Tyr
1 5

(2) INFORMATION FOR SEQ ID NO: 56:

(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 6 amino acids
(B) TYPE: amino acid
(D) TOPOLOGY: linear

(ii) MOLECULE TYPE: peptide

(v) FRAGMENT TYPE: internal

(ix) FEATURE:
(A) NAME/KEY: Peptide
(B) LOCATION: 1..6
(D) OTHER INFORMATION: /note= "52-57 REGION OF HUMAN IGF-I"

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 56:

Cys Asp Leu Arg Arg Leu
1 5

(2) INFORMATION FOR SEQ ID NO: 57:

(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 6 amino acids
(B) TYPE: amino acid
(D) TOPOLOGY: linear

(ii) MOLECULE TYPE: peptide

(v) FRAGMENT TYPE: internal

(ix) FEATURE:
(A) NAME/KEY: Peptide
(B) LOCATION: 1..6
(D) OTHER INFORMATION: /note= "53-58 REGION OF HUMAN IGF-I"

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 57:

Asp Leu Arg Arg Leu Glu
1 5

(2) INFORMATION FOR SEQ ID NO: 58:

(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 6 amino acids
(B) TYPE: amino acid
(D) TOPOLOGY: linear

(ii) MOLECULE TYPE: peptide

(v) FRAGMENT TYPE: internal

(ix) FEATURE:
(A) NAME/KEY: Peptide
(B) LOCATION: 1..6
(D) OTHER INFORMATION: /note= "54-59 REGION OF HUMAN IGF-I"

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 58:

Leu Arg Arg Leu Glu Met
1 5

(2) INFORMATION FOR SEQ ID NO: 59:

(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 6 amino acids
(B) TYPE: amino acid
(D) TOPOLOGY: linear

(ii) MOLECULE TYPE: peptide

(v) FRAGMENT TYPE: internal

(ix) FEATURE:
(A) NAME/KEY: Peptide
(B) LOCATION: 1..6
(D) OTHER INFORMATION: /note= "55-60 REGION OF HUMAN IGF-I"

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 59:

Arg Arg Leu Glu Met Tyr
1 5

(2) INFORMATION FOR SEQ ID NO: 60:

(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 6 amino acids
(B) TYPE: amino acid
(D) TOPOLOGY: linear

(ii) MOLECULE TYPE: peptide

(v) FRAGMENT TYPE: internal

(ix) FEATURE:
(A) NAME/KEY: Peptide
(B) LOCATION: 1..6
(D) OTHER INFORMATION: /note= "56-61 REGION OF HUMAN IGF-I"

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 60:

Arg Leu Glu Met Tyr Cys
1 5

(2) INFORMATION FOR SEQ ID NO: 61:

(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 6 amino acids
(B) TYPE: amino acid
(D) TOPOLOGY: linear

(ii) MOLECULE TYPE: peptide

(v) FRAGMENT TYPE: internal

(ix) FEATURE:
(A) NAME/KEY: Peptide
(B) LOCATION: 1..6
(D) OTHER INFORMATION: /note= "57-62 REGION OF HUMAN IGF-I"

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 61:

Leu Glu Met Tyr Cys Ala
1 5

(2) INFORMATION FOR SEQ ID NO: 62:

(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 7 amino acids
(B) TYPE: amino acid
(D) TOPOLOGY: linear

(ii) MOLECULE TYPE: peptide

(v) FRAGMENT TYPE: N-terminal

(ix) FEATURE:
(A) NAME/KEY: Peptide
(B) LOCATION: 1..7
(D) OTHER INFORMATION: /note= "1-7 REGION OF HUMAN IGF-I"

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 62:

Gly Pro Glu Thr Leu Cys Gly
1 5

(2) INFORMATION FOR SEQ ID NO: 63:

(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 7 amino acids
(B) TYPE: amino acid
(D) TOPOLOGY: linear

(ii) MOLECULE TYPE: peptide

(v) FRAGMENT TYPE: internal

(ix) FEATURE:
(A) NAME/KEY: Peptide
(B) LOCATION: 1..7
(D) OTHER INFORMATION: /note= "2-8 REGION OF HUMAN IGF-I"

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 63:

Pro Glu Thr Leu Cys Gly Ala
1 5

(2) INFORMATION FOR SEQ ID NO: 64:

(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 7 amino acids
(B) TYPE: amino acid
(D) TOPOLOGY: linear

(ii) MOLECULE TYPE: peptide

(v) FRAGMENT TYPE: internal

(ix) FEATURE:
(A) NAME/KEY: Peptide
(B) LOCATION: 1..7
(D) OTHER INFORMATION: /note= "3-9 REGION OF HUMAN IGF-I"

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 64:

Glu Thr Leu Cys Gly Ala Glu
1 5

(2) INFORMATION FOR SEQ ID NO: 65:

(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 7 amino acids
(B) TYPE: amino acid
(D) TOPOLOGY: linear

(ii) MOLECULE TYPE: peptide

(v) FRAGMENT TYPE: internal

(ix) FEATURE:
(A) NAME/KEY: Peptide
(B) LOCATION: 1..7
(D) OTHER INFORMATION: /note= "4-10 REGION OF HUMAN IGF-I"

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 65:

Thr Leu Cys Gly Ala Glu Leu
1 5

(2) INFORMATION FOR SEQ ID NO: 66:

(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 7 amino acids
(B) TYPE: amino acid
(D) TOPOLOGY: linear

(ii) MOLECULE TYPE: peptide

(v) FRAGMENT TYPE: internal

(ix) FEATURE:
(A) NAME/KEY: Peptide
(B) LOCATION: 1..7
(D) OTHER INFORMATION: /note= "5-11 REGION OF HUMAN IGF-I"

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 66:

Leu Cys Gly Ala Glu Leu Val
1 5

(2) INFORMATION FOR SEQ ID NO: 67:

(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 7 amino acids
(B) TYPE: amino acid
(D) TOPOLOGY: linear

(ii) MOLECULE TYPE: peptide

(v) FRAGMENT TYPE: internal

(ix) FEATURE:
(A) NAME/KEY: Peptide
(B) LOCATION: 1..7
(D) OTHER INFORMATION: /note= "6-12 REGION OF HUMAN IGF-I"

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 67:

Cys Gly Ala Glu Leu Val Asp
1 5

(2) INFORMATION FOR SEQ ID NO: 68:

(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 7 amino acids
(B) TYPE: amino acid
(D) TOPOLOGY: linear

(ii) MOLECULE TYPE: peptide

(v) FRAGMENT TYPE: internal

(ix) FEATURE:
(A) NAME/KEY: Peptide
(B) LOCATION: 1..7
(D) OTHER INFORMATION: /note= "7-13 REGION OF HUMAN IGF-I"

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 68:

Gly Ala Glu Leu Val Asp Ala
1 5

(2) INFORMATION FOR SEQ ID NO: 69:

(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 7 amino acids
(B) TYPE: amino acid
(D) TOPOLOGY: linear

(ii) MOLECULE TYPE: peptide

(v) FRAGMENT TYPE: internal

(ix) FEATURE:
(A) NAME/KEY: Peptide
(B) LOCATION: 1..7
(D) OTHER INFORMATION: /note= "8-14 REGION OF HUMAN IGF-I"

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 69:

Ala Glu Leu Val Asp Ala Leu
1 5

(2) INFORMATION FOR SEQ ID NO: 70:

(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 7 amino acids
(B) TYPE: amino acid
(D) TOPOLOGY: linear

(ii) MOLECULE TYPE: peptide

(v) FRAGMENT TYPE: internal

(ix) FEATURE:
(A) NAME/KEY: Peptide
(B) LOCATION: 1..7
(D) OTHER INFORMATION: /note= "9-15 REGION OF HUMAN IGF-I"

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 70:

Glu Leu Val Asp Ala Leu Gln
1 5

(2) INFORMATION FOR SEQ ID NO: 71:

(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 7 amino acids
(B) TYPE: amino acid
(D) TOPOLOGY: linear

(ii) MOLECULE TYPE: peptide

(v) FRAGMENT TYPE: internal

(ix) FEATURE:
(A) NAME/KEY: Peptide
(B) LOCATION: 1..7
(D) OTHER INFORMATION: /note= "10-16 REGION OF HUMAN IGF-I"

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 71:

Leu Val Asp Ala Leu Gln Phe
1 5

(2) INFORMATION FOR SEQ ID NO: 72:

(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 7 amino acids
(B) TYPE: amino acid
(D) TOPOLOGY: linear

(ii) MOLECULE TYPE: peptide

(v) FRAGMENT TYPE: internal

(ix) FEATURE:
(A) NAME/KEY: Peptide
(B) LOCATION: 1..7
(D) OTHER INFORMATION: /note= "11-17 REGION OF HUMAN IGF-I"

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 72:

Val Asp Ala Leu Gln Phe Val
1 5

(2) INFORMATION FOR SEQ ID NO: 73:

(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 7 amino acids
(B) TYPE: amino acid
(D) TOPOLOGY: linear

(ii) MOLECULE TYPE: peptide

(v) FRAGMENT TYPE: internal

(ix) FEATURE:
(A) NAME/KEY: Peptide
(B) LOCATION: 1..7
(D) OTHER INFORMATION: /note= "12-18 REGION OF HUMAN IGF-I"

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 73:

Asp Ala Leu Gln Phe Val Cys
1 5

(2) INFORMATION FOR SEQ ID NO: 74:

(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 7 amino acids
(B) TYPE: amino acid
(D) TOPOLOGY: linear

(ii) MOLECULE TYPE: peptide

(v) FRAGMENT TYPE: internal

(ix) FEATURE:
(A) NAME/KEY: Peptide
(B) LOCATION: 1..7
(D) OTHER INFORMATION: /note= "13-19 REGION OF HUMAN IGF-I"

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 74:

Ala Leu Gln Phe Val Cys Gly
1 5

(2) INFORMATION FOR SEQ ID NO: 75:

(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 7 amino acids
(B) TYPE: amino acid
(D) TOPOLOGY: linear

(ii) MOLECULE TYPE: peptide

(v) FRAGMENT TYPE: internal

(ix) FEATURE:
(A) NAME/KEY: Peptide
(B) LOCATION: 1..7
(D) OTHER INFORMATION: /note= "14-20 REGION OF HUMAN IGF-I"

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 75:

Leu Gln Phe Val Cys Gly Asp
1 5

(2) INFORMATION FOR SEQ ID NO: 76:

(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 7 amino acids
(B) TYPE: amino acid
(D) TOPOLOGY: linear

(ii) MOLECULE TYPE: peptide

(v) FRAGMENT TYPE: internal

(ix) FEATURE:
(A) NAME/KEY: Peptide
(B) LOCATION: 1..7
(D) OTHER INFORMATION: /note= "15-21 REGION OF HUMAN IGF-I"

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 76:

Gln Phe Val Cys Gly Asp Arg
1 5

(2) INFORMATION FOR SEQ ID NO: 77:

(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 7 amino acids
(B) TYPE: amino acid
(D) TOPOLOGY: linear

(ii) MOLECULE TYPE: peptide

(v) FRAGMENT TYPE: internal

(ix) FEATURE:
(A) NAME/KEY: Peptide
(B) LOCATION: 1..7
(D) OTHER INFORMATION: /note= "16-22 REGION OF HUMAN IGF-I"

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 77:

Phe Val Cys Gly Asp Arg Gly
1 5

(2) INFORMATION FOR SEQ ID NO: 78:

(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 7 amino acids
(B) TYPE: amino acid
(D) TOPOLOGY: linear

(ii) MOLECULE TYPE: peptide

(v) FRAGMENT TYPE: internal

(ix) FEATURE:
(A) NAME/KEY: Peptide
(B) LOCATION: 1..7
(D) OTHER INFORMATION: /note= "17-23 REGION OF HUMAN IGF-I"

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 78:

Val Cys Gly Asp Arg Gly Phe
1 5

(2) INFORMATION FOR SEQ ID NO: 79:

(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 7 amino acids
(B) TYPE: amino acid
(D) TOPOLOGY: linear

(ii) MOLECULE TYPE: peptide

(v) FRAGMENT TYPE: internal

(ix) FEATURE:
(A) NAME/KEY: Peptide
(B) LOCATION: 1..7
(D) OTHER INFORMATION: /note= "18-24 REGION OF HUMAN IGF-I"

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 79:

Cys Gly Asp Arg Gly Phe Tyr
1 5

(2) INFORMATION FOR SEQ ID NO: 80:

(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 7 amino acids
(B) TYPE: amino acid
(D) TOPOLOGY: linear

(ii) MOLECULE TYPE: peptide

(v) FRAGMENT TYPE: internal

(ix) FEATURE:
(A) NAME/KEY: Peptide
(B) LOCATION: 1..7
(D) OTHER INFORMATION: /note= "19-25 REGION OF HUMAN IGF-I"

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 80:

Gly Asp Arg Gly Phe Tyr Phe
1 5

(2) INFORMATION FOR SEQ ID NO: 81:

(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 7 amino acids
(B) TYPE: amino acid
(D) TOPOLOGY: linear

(ii) MOLECULE TYPE: peptide

(v) FRAGMENT TYPE: internal

(ix) FEATURE:
(A) NAME/KEY: Peptide
(B) LOCATION: 1..7
(D) OTHER INFORMATION: /note= "20-26 REGION OF HUMAN IGF-I"

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 81:

Asp Arg Gly Phe Tyr Phe Asn
1 5

(2) INFORMATION FOR SEQ ID NO: 82:

(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 7 amino acids
(B) TYPE: amino acid
(D) TOPOLOGY: linear

(ii) MOLECULE TYPE: peptide

(v) FRAGMENT TYPE: internal

(ix) FEATURE:
(A) NAME/KEY: Peptide
(B) LOCATION: 1..7
(D) OTHER INFORMATION: /note= "21-27 REGION OF HUMAN IGF-I"

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 82:

Arg Gly Phe Tyr Phe Asn Lys
1 5

(2) INFORMATION FOR SEQ ID NO: 83:

(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 7 amino acids
(B) TYPE: amino acid
(D) TOPOLOGY: linear

(ii) MOLECULE TYPE: peptide

(v) FRAGMENT TYPE: internal

(ix) FEATURE:
(A) NAME/KEY: Peptide
(B) LOCATION: 1..7
(D) OTHER INFORMATION: /note= "22-28 REGION OF HUMAN IGF-I"

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 83:

Gly Phe Tyr Phe Asn Lys Pro
1 5

(2) INFORMATION FOR SEQ ID NO: 84:

(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 7 amino acids
(B) TYPE: amino acid
(D) TOPOLOGY: linear

(ii) MOLECULE TYPE: peptide

(v) FRAGMENT TYPE: internal

(ix) FEATURE:
(A) NAME/KEY: Peptide
(B) LOCATION: 1..7
(D) OTHER INFORMATION: /note= "23-29 REGION OF HUMAN IGF-I"

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 84:

Phe Tyr Phe Asn Lys Pro Thr
1 5

(2) INFORMATION FOR SEQ ID NO: 85:

(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 7 amino acids
(B) TYPE: amino acid
(D) TOPOLOGY: linear

(ii) MOLECULE TYPE: peptide

(v) FRAGMENT TYPE: internal

(ix) FEATURE:
(A) NAME/KEY: Peptide
(B) LOCATION: 1..7
(D) OTHER INFORMATION: /note= "24-30 REGION OF HUMAN IGF-I"

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 85:

Tyr Phe Asn Lys Pro Thr Gly
1 5

(2) INFORMATION FOR SEQ ID NO: 86:

(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 7 amino acids
(B) TYPE: amino acid
(D) TOPOLOGY: linear

(ii) MOLECULE TYPE: peptide

(v) FRAGMENT TYPE: internal

(ix) FEATURE:
(A) NAME/KEY: Peptide
(B) LOCATION: 1..7
(D) OTHER INFORMATION: /note= "25-31 REGION OF HUMAN IGF-I"

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 86:

Phe Asn Lys Pro Thr Gly Tyr
1 5

(2) INFORMATION FOR SEQ ID NO: 87:

(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 7 amino acids
(B) TYPE: amino acid
(D) TOPOLOGY: linear

(ii) MOLECULE TYPE: peptide

(v) FRAGMENT TYPE: internal

(ix) FEATURE:
(A) NAME/KEY: Peptide
(B) LOCATION: 1..7
(D) OTHER INFORMATION: /note= "26-32 REGION OF HUMAN IGF-I"

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 87:

Asn Lys Pro Thr Gly Tyr Gly
1 5

(2) INFORMATION FOR SEQ ID NO: 88:

(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 7 amino acids
(B) TYPE: amino acid
(D) TOPOLOGY: linear

(ii) MOLECULE TYPE: peptide

(v) FRAGMENT TYPE: internal

(ix) FEATURE:
(A) NAME/KEY: Peptide
(B) LOCATION: 1..7
(D) OTHER INFORMATION: /note= "27-33 REGION OF HUMAN IGF-I"

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 88:

Lys Pro Thr Gly Tyr Gly Ser
1 5

(2) INFORMATION FOR SEQ ID NO: 89:

(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 7 amino acids
(B) TYPE: amino acid
(D) TOPOLOGY: linear

(ii) MOLECULE TYPE: peptide

(v) FRAGMENT TYPE: internal

(ix) FEATURE:
(A) NAME/KEY: Peptide
(B) LOCATION: 1..7
(D) OTHER INFORMATION: /note= "28-34 REGION OF HUMAN IGF-I"

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 89:

Pro Thr Gly Tyr Gly Ser Ser
1 5

(2) INFORMATION FOR SEQ ID NO: 90:

(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 7 amino acids
(B) TYPE: amino acid
(D) TOPOLOGY: linear

(ii) MOLECULE TYPE: peptide

(v) FRAGMENT TYPE: internal

(ix) FEATURE:
(A) NAME/KEY: Peptide
(B) LOCATION: 1..7
(D) OTHER INFORMATION: /note= "29-35 REGION OF HUMAN IGF-I"

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 90:

Thr Gly Tyr Gly Ser Ser Ser
1 5

(2) INFORMATION FOR SEQ ID NO: 91:

(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 7 amino acids
(B) TYPE: amino acid
(D) TOPOLOGY: linear

(ii) MOLECULE TYPE: peptide

(v) FRAGMENT TYPE: internal

(ix) FEATURE:
(A) NAME/KEY: Peptide
(B) LOCATION: 1..7
(D) OTHER INFORMATION: /note= "30-36 REGION OF HUMAN IGF-I"

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 91:

Gly Tyr Gly Ser Ser Ser Arg
1 5

(2) INFORMATION FOR SEQ ID NO: 92:

(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 7 amino acids
(B) TYPE: amino acid
(D) TOPOLOGY: linear

(ii) MOLECULE TYPE: peptide

(v) FRAGMENT TYPE: internal

(ix) FEATURE:
(A) NAME/KEY: Peptide
(B) LOCATION: 1..7
(D) OTHER INFORMATION: /note= "31-37 REGION OF HUMAN IGF-I"

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 92:

Tyr Gly Ser Ser Ser Arg Arg
1 5

(2) INFORMATION FOR SEQ ID NO: 93:

(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 7 amino acids
(B) TYPE: amino acid
(D) TOPOLOGY: linear

(ii) MOLECULE TYPE: peptide

(v) FRAGMENT TYPE: internal

(ix) FEATURE:
(A) NAME/KEY: Peptide
(B) LOCATION: 1..7
(D) OTHER INFORMATION: /note= "32-38 REGION OF HUMAN IGF-I"

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 93:

Gly Ser Ser Ser Arg Arg Ala
1 5

(2) INFORMATION FOR SEQ ID NO: 94:

(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 7 amino acids
(B) TYPE: amino acid
(D) TOPOLOGY: linear

(ii) MOLECULE TYPE: peptide

(v) FRAGMENT TYPE: internal

(ix) FEATURE:
(A) NAME/KEY: Peptide
(B) LOCATION: 1..7
(D) OTHER INFORMATION: /note= "33-39 REGION OF HUMAN IGF-I"

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 94:

Ser Ser Ser Arg Arg Ala Pro
1 5

(2) INFORMATION FOR SEQ ID NO: 95:

(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 7 amino acids
(B) TYPE: amino acid
(D) TOPOLOGY: linear

(ii) MOLECULE TYPE: peptide

(v) FRAGMENT TYPE: internal

(ix) FEATURE:
(A) NAME/KEY: Peptide
(B) LOCATION: 1..7
(D) OTHER INFORMATION: /note= "34-40 REGION OF HUMAN IGF-I"

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 95:

Ser Ser Arg Arg Ala Pro Gln
1 5

(2) INFORMATION FOR SEQ ID NO: 96:

(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 7 amino acids
(B) TYPE: amino acid
(D) TOPOLOGY: linear

(ii) MOLECULE TYPE: peptide

(v) FRAGMENT TYPE: internal

(ix) FEATURE:
(A) NAME/KEY: Peptide
(B) LOCATION: 1..7
(D) OTHER INFORMATION: /note= "33-39 REGION OF HUMAN IGF-I"

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 96:

Ser Ser Ser Arg Arg Ala Pro
1 5

(2) INFORMATION FOR SEQ ID NO: 97:

(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 7 amino acids
(B) TYPE: amino acid
(D) TOPOLOGY: linear

(ii) MOLECULE TYPE: peptide

(v) FRAGMENT TYPE: internal

(ix) FEATURE:
(A) NAME/KEY: Peptide
(B) LOCATION: 1..7
(D) OTHER INFORMATION: /note= "34-40 REGION OF HUMAN IGF-I"

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 97:

Ser Ser Arg Arg Ala Pro Gln
1 5

(2) INFORMATION FOR SEQ ID NO: 98:

(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 7 amino acids
(B) TYPE: amino acid
(D) TOPOLOGY: linear

(ii) MOLECULE TYPE: peptide

(v) FRAGMENT TYPE: internal

(ix) FEATURE:
(A) NAME/KEY: Peptide
(B) LOCATION: 1..7
(D) OTHER INFORMATION: /note= "35-41 REGION OF HUMAN IGF-I"

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 98:

Ser Arg Arg Ala Pro Gln Thr
1 5

(2) INFORMATION FOR SEQ ID NO: 99:

(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 7 amino acids
(B) TYPE: amino acid
(D) TOPOLOGY: linear

(ii) MOLECULE TYPE: peptide

(v) FRAGMENT TYPE: internal

(ix) FEATURE:
(A) NAME/KEY: Peptide
(B) LOCATION: 1..7
(D) OTHER INFORMATION: /note= "36-42 REGION OF HUMAN IGF-I"

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 99:

Arg Arg Ala Pro Gln Thr Gly
1 5

(2) INFORMATION FOR SEQ ID NO:100:

(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 7 amino acids
(B) TYPE: amino acid
(D) TOPOLOGY: linear

(ii) MOLECULE TYPE: peptide

(v) FRAGMENT TYPE: internal

(ix) FEATURE:
(A) NAME/KEY: Peptide
(B) LOCATION: 1..7
(D) OTHER INFORMATION: /note= "37-43 REGION OF HUMAN IGF-I"

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:100:

Arg Ala Pro Gln Thr Gly Ile
1 5

(2) INFORMATION FOR SEQ ID NO:101:

(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 7 amino acids
(B) TYPE: amino acid
(D) TOPOLOGY: linear

(ii) MOLECULE TYPE: peptide

(v) FRAGMENT TYPE: internal

(ix) FEATURE:
(A) NAME/KEY: Peptide
(B) LOCATION: 1..7
(D) OTHER INFORMATION: /note= "37-43 REGION OF HUMAN IGF-I"

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:101:

Ala Pro Gln Thr Gly Ile Val
1 5

(2) INFORMATION FOR SEQ ID NO:102:

(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 7 amino acids
(B) TYPE: amino acid
(D) TOPOLOGY: linear

(ii) MOLECULE TYPE: peptide

(v) FRAGMENT TYPE: internal

(ix) FEATURE:
(A) NAME/KEY: Peptide
(B) LOCATION: 1..7
(D) OTHER INFORMATION: /note= "38-44 REGION OF HUMAN IGF-I"

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:102:

Pro Gln Thr Gly Ile Val Asp
1 5

(2) INFORMATION FOR SEQ ID NO:103:

(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 7 amino acids
(B) TYPE: amino acid
(D) TOPOLOGY: linear

(ii) MOLECULE TYPE: peptide

(v) FRAGMENT TYPE: internal

(ix) FEATURE:
(A) NAME/KEY: Peptide
(B) LOCATION: 1..7
(D) OTHER INFORMATION: /note= "39-45 REGION OF HUMAN IGF-I"

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:103:

Gln Thr Gly Ile Val Asp Glu
1 5

(2) INFORMATION FOR SEQ ID NO:104:

(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 7 amino acids
(B) TYPE: amino acid
(D) TOPOLOGY: linear

(ii) MOLECULE TYPE: peptide

(v) FRAGMENT TYPE: internal

(ix) FEATURE:
(A) NAME/KEY: Peptide
(B) LOCATION: 1..7
(D) OTHER INFORMATION: /note= "40-46 REGION OF HUMAN IGF-I"

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:104:

Thr Gly Ile Val Asp Glu Cys
1 5

(2) INFORMATION FOR SEQ ID NO:105:

(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 7 amino acids
(B) TYPE: amino acid
(D) TOPOLOGY: linear

(ii) MOLECULE TYPE: peptide

(v) FRAGMENT TYPE: internal

(ix) FEATURE:
(A) NAME/KEY: Peptide
(B) LOCATION: 1..7
(D) OTHER INFORMATION: /note= "42-48 REGION OF HUMAN IGF-I"

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:105:

Gly Ile Val Asp Glu Cys Cys
1 5

(2) INFORMATION FOR SEQ ID NO:106:

(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 7 amino acids
(B) TYPE: amino acid
(D) TOPOLOGY: linear

(ii) MOLECULE TYPE: peptide

(v) FRAGMENT TYPE: internal

(ix) FEATURE:
(A) NAME/KEY: Peptide
(B) LOCATION: 1..7
(D) OTHER INFORMATION: /note= "43-49 REGION OF HUMAN IGF-I"

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:106:

Ile Val Asp Glu Cys Cys Phe
1 5

(2) INFORMATION FOR SEQ ID NO:107:

(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 7 amino acids
(B) TYPE: amino acid
(D) TOPOLOGY: linear

(ii) MOLECULE TYPE: peptide

(v) FRAGMENT TYPE: internal

(ix) FEATURE:
(A) NAME/KEY: Peptide
(B) LOCATION: 1..7
(D) OTHER INFORMATION: /note= "44-50 REGION OF HUMAN IGF-I"

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:107:

Val Asp Glu Cys Cys Phe Arg
1 5

(2) INFORMATION FOR SEQ ID NO:108:

(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 7 amino acids
(B) TYPE: amino acid
(D) TOPOLOGY: linear

(ii) MOLECULE TYPE: peptide

(v) FRAGMENT TYPE: internal

(ix) FEATURE:
(A) NAME/KEY: Peptide
(B) LOCATION: 1..7
(D) OTHER INFORMATION: /note= "45-51 REGION OF HUMAN IGF-I"

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:108:

Asp Glu Cys Cys Phe Arg Ser
1 5

(2) INFORMATION FOR SEQ ID NO:109:

(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 7 amino acids
(B) TYPE: amino acid
(D) TOPOLOGY: linear

(ii) MOLECULE TYPE: peptide

(v) FRAGMENT TYPE: internal

(ix) FEATURE:
(A) NAME/KEY: Peptide
(B) LOCATION: 1..7
(D) OTHER INFORMATION: /note= "46-52 REGION OF HUMAN IGF-I"

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:109:

Glu Cys Cys Phe Arg Ser Cys
1 5

(2) INFORMATION FOR SEQ ID NO:110:

(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 7 amino acids
(B) TYPE: amino acid
(D) TOPOLOGY: linear

(ii) MOLECULE TYPE: peptide

(v) FRAGMENT TYPE: internal

(ix) FEATURE:
(A) NAME/KEY: Peptide
(B) LOCATION: 1..7
(D) OTHER INFORMATION: /note= "47-53 REGION OF HUMAN IGF-I"

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:110:

Cys Cys Phe Arg Ser Cys Asp
1 5

(2) INFORMATION FOR SEQ ID NO:111:

(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 7 amino acids
(B) TYPE: amino acid
(D) TOPOLOGY: linear

(ii) MOLECULE TYPE: peptide

(v) FRAGMENT TYPE: internal

(ix) FEATURE:
(A) NAME/KEY: Peptide
(B) LOCATION: 1..7
(D) OTHER INFORMATION: /note= "48-54 REGION OF HUMAN IGF-I"

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:111:

Cys Phe Arg Ser Cys Asp Leu
1 5

(2) INFORMATION FOR SEQ ID NO:112:

(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 7 amino acids
(B) TYPE: amino acid
(D) TOPOLOGY: linear

(ii) MOLECULE TYPE: peptide

(v) FRAGMENT TYPE: internal

(ix) FEATURE:
(A) NAME/KEY: Peptide
(B) LOCATION: 1..7
(D) OTHER INFORMATION: /note= "49-55 REGION OF HUMAN IGF-I"

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:112:

Phe Arg Ser Cys Asp Leu Arg
1 5

(2) INFORMATION FOR SEQ ID NO:113:

(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 7 amino acids
(B) TYPE: amino acid
(D) TOPOLOGY: linear

(ii) MOLECULE TYPE: peptide

(v) FRAGMENT TYPE: internal

(ix) FEATURE:
(A) NAME/KEY: Peptide
(B) LOCATION: 1..7
(D) OTHER INFORMATION: /note= "50-56 REGION OF HUMAN IGF-I"

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:113:

Arg Ser Cys Asp Leu Arg Arg
1 5

(2) INFORMATION FOR SEQ ID NO:114:

(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 7 amino acids
(B) TYPE: amino acid
(D) TOPOLOGY: linear

(ii) MOLECULE TYPE: peptide

(v) FRAGMENT TYPE: internal

(ix) FEATURE:
(A) NAME/KEY: Peptide
(B) LOCATION: 1..7
(D) OTHER INFORMATION: /note= "51-57 REGION OF HUMAN IGF-I"

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:114:

Ser Cys Asp Leu Arg Arg Leu
1 5

(2) INFORMATION FOR SEQ ID NO:115:

(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 7 amino acids
(B) TYPE: amino acid
(D) TOPOLOGY: linear

(ii) MOLECULE TYPE: peptide

(v) FRAGMENT TYPE: internal

(ix) FEATURE:
(A) NAME/KEY: Peptide
(B) LOCATION: 1..7
(D) OTHER INFORMATION: /note= "52-58 REGION OF HUMAN IGF-I"

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:115:

Cys Asp Leu Arg Arg Leu Glu
1 5

(2) INFORMATION FOR SEQ ID NO:116:

(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 7 amino acids
(B) TYPE: amino acid
(D) TOPOLOGY: linear

(ii) MOLECULE TYPE: peptide

(v) FRAGMENT TYPE: internal

(ix) FEATURE:
(A) NAME/KEY: Peptide
(B) LOCATION: 1..7
(D) OTHER INFORMATION: /note= "53-59 REGION OF HUMAN IGF-I"

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:116:

Asp Leu Arg Arg Leu Glu Met
1 5

(2) INFORMATION FOR SEQ ID NO:117:

(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 7 amino acids
(B) TYPE: amino acid
(D) TOPOLOGY: linear

(ii) MOLECULE TYPE: peptide

(v) FRAGMENT TYPE: internal

(ix) FEATURE:
(A) NAME/KEY: Peptide
(B) LOCATION: 1..7
(D) OTHER INFORMATION: /note= "54-60 REGION OF HUMAN IGF-I"

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:117:

Leu Arg Arg Leu Glu Met Tyr
1 5

(2) INFORMATION FOR SEQ ID NO:118:

(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 7 amino acids
(B) TYPE: amino acid
(D) TOPOLOGY: linear

(ii) MOLECULE TYPE: peptide

(v) FRAGMENT TYPE: internal

(ix) FEATURE:
(A) NAME/KEY: Peptide
(B) LOCATION: 1..7
(D) OTHER INFORMATION: /note= "55-61 REGION OF HUMAN IGF-I"

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:118:

Arg Arg Leu Glu Met Tyr Cys
1 5

(2) INFORMATION FOR SEQ ID NO:119:

(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 7 amino acids
(B) TYPE: amino acid
(D) TOPOLOGY: linear

(ii) MOLECULE TYPE: peptide

(v) FRAGMENT TYPE: internal

(ix) FEATURE:
(A) NAME/KEY: Peptide
(B) LOCATION: 1..7
(D) OTHER INFORMATION: /note= "56-62 REGION OF HUMAN IGF-I"

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:119:

Arg Leu Glu Met Tyr Cys Ala
1 5

(2) INFORMATION FOR SEQ ID NO:120:

(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 7 amino acids
(B) TYPE: amino acid
(D) TOPOLOGY: linear

(ii) MOLECULE TYPE: peptide

(v) FRAGMENT TYPE: internal

(ix) FEATURE:
(A) NAME/KEY: Peptide
(B) LOCATION: 1..7
(D) OTHER INFORMATION: /note= "57-63 REGION OF HUMAN IGF-I"

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:120:

Leu Glu Met Tyr Cys Ala Pro
1 5

(2) INFORMATION FOR SEQ ID NO:121:

(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 8 amino acids
(B) TYPE: amino acid
(D) TOPOLOGY: linear

(ii) MOLECULE TYPE: peptide

(v) FRAGMENT TYPE: N-terminal

(ix) FEATURE:
(A) NAME/KEY: Peptide
(B) LOCATION: 1..8
(D) OTHER INFORMATION: /note= "1-8 REGION OF HUMAN IGF-I"

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:121:

Gly Pro Glu Thr Leu Cys Gly Ala
1 5

(2) INFORMATION FOR SEQ ID NO:122:

(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 8 amino acids
(B) TYPE: amino acid
(D) TOPOLOGY: linear

(ii) MOLECULE TYPE: peptide

(v) FRAGMENT TYPE: internal

(ix) FEATURE:
(A) NAME/KEY: Peptide
(B) LOCATION: 1..8
(D) OTHER INFORMATION: /note= "2-9 REGION OF HUMAN IGF-I"

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:122:

Pro Glu Thr Leu Cys Gly Ala Glu
1 5

(2) INFORMATION FOR SEQ ID NO:123:

(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 8 amino acids
(B) TYPE: amino acid
(D) TOPOLOGY: linear

(ii) MOLECULE TYPE: peptide

(v) FRAGMENT TYPE: internal

(ix) FEATURE:
(A) NAME/KEY: Peptide
(B) LOCATION: 1..8
(D) OTHER INFORMATION: /note= "3-10 REGION OF HUMAN IGF-I"

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:123:

Glu Thr Leu Cys Gly Ala Glu Leu
1 5

(2) INFORMATION FOR SEQ ID NO:124:

(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 8 amino acids
(B) TYPE: amino acid
(D) TOPOLOGY: linear

(ii) MOLECULE TYPE: peptide

(v) FRAGMENT TYPE: internal

(ix) FEATURE:
(A) NAME/KEY: Peptide
(B) LOCATION: 1..8
(D) OTHER INFORMATION: /note= "4-11 REGION OF HUMAN IGF-I"

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:124:

Thr Leu Cys Gly Ala Glu Leu Val
1 5

(2) INFORMATION FOR SEQ ID NO:125:

(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 8 amino acids
(B) TYPE: amino acid
(D) TOPOLOGY: linear

(ii) MOLECULE TYPE: peptide

(v) FRAGMENT TYPE: internal

(ix) FEATURE:
(A) NAME/KEY: Peptide
(B) LOCATION: 1..8
(D) OTHER INFORMATION: /note= "5-12 REGION OF HUMAN IGF-I"

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:125:

Leu Cys Gly Ala Glu Leu Val Asp
1 5

(2) INFORMATION FOR SEQ ID NO:126:

(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 8 amino acids
(B) TYPE: amino acid
(D) TOPOLOGY: linear

(ii) MOLECULE TYPE: peptide

(v) FRAGMENT TYPE: internal

(ix) FEATURE:
(A) NAME/KEY: Peptide
(B) LOCATION: 1..8
(D) OTHER INFORMATION: /note= "6-13 REGION OF HUMAN IGF-I"

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:126:

Cys Gly Ala Glu Leu Val Asp Ala
1 5

(2) INFORMATION FOR SEQ ID NO:127:

(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 8 amino acids
(B) TYPE: amino acid
(D) TOPOLOGY: linear

(ii) MOLECULE TYPE: peptide

(v) FRAGMENT TYPE: internal

(ix) FEATURE:
(A) NAME/KEY: Peptide
(B) LOCATION: 1..8
(D) OTHER INFORMATION: /note= "7-14 REGION OF HUMAN IGF-I"

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:127:

Gly Ala Glu Leu Val Asp Ala Leu
1 5

(2) INFORMATION FOR SEQ ID NO:128:

(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 8 amino acids
(B) TYPE: amino acid
(D) TOPOLOGY: linear

(ii) MOLECULE TYPE: peptide

(v) FRAGMENT TYPE: internal

(ix) FEATURE:
(A) NAME/KEY: Peptide
(B) LOCATION: 1..8
(D) OTHER INFORMATION: /note= "8-15 REGION OF HUMAN IGF-I"

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:128:

Ala Glu Leu Val Asp Ala Leu Gln
1 5

(2) INFORMATION FOR SEQ ID NO:129:

(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 8 amino acids
(B) TYPE: amino acid
(D) TOPOLOGY: linear

(ii) MOLECULE TYPE: peptide

(v) FRAGMENT TYPE: internal

(ix) FEATURE:
(A) NAME/KEY: Peptide
(B) LOCATION: 1..8
(D) OTHER INFORMATION: /note= "9-16 REGION OF HUMAN IGF-I"

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:129:

Glu Leu Val Asp Ala Leu Gln Phe
1 5

(2) INFORMATION FOR SEQ ID NO:130:

(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 8 amino acids
(B) TYPE: amino acid
(D) TOPOLOGY: linear

(ii) MOLECULE TYPE: peptide

(v) FRAGMENT TYPE: internal

(ix) FEATURE:
(A) NAME/KEY: Peptide
(B) LOCATION: 1..8
(D) OTHER INFORMATION: /note= "10-17 REGION OF HUMAN IGF-I"

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:130:

Leu Val Asp Ala Leu Gln Phe Val
1 5

(2) INFORMATION FOR SEQ ID NO:131:

(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 8 amino acids
(B) TYPE: amino acid
(D) TOPOLOGY: linear

(ii) MOLECULE TYPE: peptide

(v) FRAGMENT TYPE: internal

(ix) FEATURE:
(A) NAME/KEY: Peptide
(B) LOCATION: 1..8
(D) OTHER INFORMATION: /note= "11-18 REGION OF HUMAN IGF-I"

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:131:

Val Asp Ala Leu Gln Phe Val Cys
1 5

(2) INFORMATION FOR SEQ ID NO:132:

(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 8 amino acids
(B) TYPE: amino acid
(D) TOPOLOGY: linear

(ii) MOLECULE TYPE: peptide

(v) FRAGMENT TYPE: internal

(ix) FEATURE:
(A) NAME/KEY: Peptide
(B) LOCATION: 1..8
(D) OTHER INFORMATION: /note= "12-19 REGION OF HUMAN IGF-I"

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:132:

Asp Ala Leu Gln Phe Val Cys Gly
1 5

(2) INFORMATION FOR SEQ ID NO:133:

(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 8 amino acids
(B) TYPE: amino acid
(D) TOPOLOGY: linear

(ii) MOLECULE TYPE: peptide

(v) FRAGMENT TYPE: internal

(ix) FEATURE:
(A) NAME/KEY: Peptide
(B) LOCATION: 1..8
(D) OTHER INFORMATION: /note= "13-20 REGION OF HUMAN IGF-I"

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:133:

Ala Leu Gln Phe Val Cys Gly Asp
1 5

(2) INFORMATION FOR SEQ ID NO:134:

(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 8 amino acids
(B) TYPE: amino acid
(D) TOPOLOGY: linear

(ii) MOLECULE TYPE: peptide

(v) FRAGMENT TYPE: internal

(ix) FEATURE:
(A) NAME/KEY: Peptide
(B) LOCATION: 1..8
(D) OTHER INFORMATION: /note= "14-21 REGION OF HUMAN IGF-I"

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:134:

Leu Gln Phe Val Cys Gly Asp Arg
1 5

(2) INFORMATION FOR SEQ ID NO:135:

(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 8 amino acids
(B) TYPE: amino acid
(D) TOPOLOGY: linear

(ii) MOLECULE TYPE: peptide

(v) FRAGMENT TYPE: internal

(ix) FEATURE:
(A) NAME/KEY: Peptide
(B) LOCATION: 1..8
(D) OTHER INFORMATION: /note= "15-22 REGION OF HUMAN IGF-I"

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:135:
Gln Phe Val Cys Gly Asp Arg Gly
1 5

(2) INFORMATION FOR SEQ ID NO:136:

(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 8 amino acids
(B) TYPE: amino acid
(D) TOPOLOGY: linear

(ii) MOLECULE TYPE: peptide

(v) FRAGMENT TYPE: internal

(ix) FEATURE:
(A) NAME/KEY: Peptide
(B) LOCATION: 1..8
(D) OTHER INFORMATION: /note= "16-23 REGION OF HUMAN IGF-I"

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:136:
Phe Val Cys Gly Asp Arg Gly Phe
1 5

(2) INFORMATION FOR SEQ ID NO:137:

(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 8 amino acids
(B) TYPE: amino acid
(D) TOPOLOGY: linear

(ii) MOLECULE TYPE: peptide

(v) FRAGMENT TYPE: internal

(ix) FEATURE:
(A) NAME/KEY: Peptide
(B) LOCATION: 1..8
(D) OTHER INFORMATION: /note= "17-24 REGION OF HUMAN IGF-I"

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:137:
Val Cys Gly Asp Arg Gly Phe Tyr
1 5

(2) INFORMATION FOR SEQ ID NO:138:

(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 8 amino acids
(B) TYPE: amino acid
(D) TOPOLOGY: linear

(ii) MOLECULE TYPE: peptide

(v) FRAGMENT TYPE: internal

(ix) FEATURE:
(A) NAME/KEY: Peptide
(B) LOCATION: 1..8
(D) OTHER INFORMATION: /note= "18-25 REGION OF HUMAN IGF-I"

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:138:
Cys Gly Asp Arg Gly Phe Tyr Phe
1 5

(2) INFORMATION FOR SEQ ID NO:139:

(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 8 amino acids
(B) TYPE: amino acid
(D) TOPOLOGY: linear

(ii) MOLECULE TYPE: peptide

(v) FRAGMENT TYPE: internal

(ix) FEATURE:
(A) NAME/KEY: Peptide
(B) LOCATION: 1..8
(D) OTHER INFORMATION: /note= "19-26 REGION OF HUMAN IGF-I"

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:139:
Gly Asp Arg Gly Phe Tyr Phe Asn
1 5

(2) INFORMATION FOR SEQ ID NO:140:

(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 8 amino acids
(B) TYPE: amino acid
(D) TOPOLOGY: linear

(ii) MOLECULE TYPE: peptide

(v) FRAGMENT TYPE: internal

(ix) FEATURE:
(A) NAME/KEY: Peptide
(B) LOCATION: 1..8
(D) OTHER INFORMATION: /note= "20-27 REGION OF HUMAN IGF-I"

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:140:
Asp Arg Gly Phe Tyr Phe Asn Lys
1 5

(2) INFORMATION FOR SEQ ID NO:141:

(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 8 amino acids
(B) TYPE: amino acid
(D) TOPOLOGY: linear

(ii) MOLECULE TYPE: peptide

(v) FRAGMENT TYPE: internal

(ix) FEATURE:
(A) NAME/KEY: Peptide
(B) LOCATION: 1..8
(D) OTHER INFORMATION: /note= "21-28 REGION OF HUMAN IGF-I"

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:141:

Arg Gly Phe Tyr Phe Asn Lys Pro
1 5

(2) INFORMATION FOR SEQ ID NO:142:

(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 8 amino acids
(B) TYPE: amino acid
(D) TOPOLOGY: linear

(ii) MOLECULE TYPE: peptide

(v) FRAGMENT TYPE: internal

(ix) FEATURE:
(A) NAME/KEY: Peptide
(B) LOCATION: 1..8
(D) OTHER INFORMATION: /note= "22-29 REGION OF HUMAN IGF-I"

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:142:

Gly Phe Tyr Phe Asn Lys Pro Thr
1 5

(2) INFORMATION FOR SEQ ID NO:143:

(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 8 amino acids
(B) TYPE: amino acid
(D) TOPOLOGY: linear

(ii) MOLECULE TYPE: peptide

(v) FRAGMENT TYPE: internal

(ix) FEATURE:
(A) NAME/KEY: Peptide
(B) LOCATION: 1..8
(D) OTHER INFORMATION: /note= "23-30 REGION OF HUMAN IGF-I"

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:143:

Phe Tyr Phe Asn Lys Pro Thr Gly
1 5

(2) INFORMATION FOR SEQ ID NO:144:

(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 8 amino acids
(B) TYPE: amino acid
(D) TOPOLOGY: linear

(ii) MOLECULE TYPE: peptide

(v) FRAGMENT TYPE: internal

(ix) FEATURE:
(A) NAME/KEY: Peptide
(B) LOCATION: 1..8
(D) OTHER INFORMATION: /note= "24-31 REGION OF HUMAN IGF-I"

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:144:

Tyr Phe Asn Lys Pro Thr Gly Tyr
1 5

(2) INFORMATION FOR SEQ ID NO:145:

(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 8 amino acids
(B) TYPE: amino acid
(D) TOPOLOGY: linear

(ii) MOLECULE TYPE: peptide

(v) FRAGMENT TYPE: internal

(ix) FEATURE:
(A) NAME/KEY: Peptide
(B) LOCATION: 1..8
(D) OTHER INFORMATION: /note= "25-32 REGION OF HUMAN IGF-I"

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:145:

Phe Asn Lys Pro Thr Gly Tyr Gly
1 5

(2) INFORMATION FOR SEQ ID NO:146:

(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 8 amino acids
(B) TYPE: amino acid
(D) TOPOLOGY: linear

(ii) MOLECULE TYPE: peptide

(v) FRAGMENT TYPE: internal

(ix) FEATURE:
(A) NAME/KEY: Peptide
(B) LOCATION: 1..8
(D) OTHER INFORMATION: /note= "26-33 REGION OF HUMAN IGF-I"

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:146:

Asn Lys Pro Thr Gly Tyr Gly Ser
1 5

(2) INFORMATION FOR SEQ ID NO:147:

(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 8 amino acids
(B) TYPE: amino acid
(D) TOPOLOGY: linear

(ii) MOLECULE TYPE: peptide

(v) FRAGMENT TYPE: internal

(ix) FEATURE:
(A) NAME/KEY: Peptide
(B) LOCATION: 1..8
(D) OTHER INFORMATION: /note= "27-34 REGION OF HUMAN IGF-I"

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:147:

Lys Pro Thr Gly Tyr Gly Ser Ser
1 5

(2) INFORMATION FOR SEQ ID NO:148:

(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 8 amino acids
(B) TYPE: amino acid
(D) TOPOLOGY: linear

(ii) MOLECULE TYPE: peptide

(v) FRAGMENT TYPE: internal

(ix) FEATURE:
(A) NAME/KEY: Peptide
(B) LOCATION: 1..8
(D) OTHER INFORMATION: /note= "28-35 REGION OF HUMAN IGF-I"

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:148:

Pro Thr Gly Tyr Gly Ser Ser Ser
1 5

(2) INFORMATION FOR SEQ ID NO:149:

(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 8 amino acids
(B) TYPE: amino acid
(D) TOPOLOGY: linear

(ii) MOLECULE TYPE: peptide

(v) FRAGMENT TYPE: internal

(ix) FEATURE:
(A) NAME/KEY: Peptide
(B) LOCATION: 1..8
(D) OTHER INFORMATION: /note= "29-36 REGION OF HUMAN IGF-I"

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:149:

Thr Gly Tyr Gly Ser Ser Ser Arg
1 5

(2) INFORMATION FOR SEQ ID NO:150:

(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 8 amino acids
(B) TYPE: amino acid
(D) TOPOLOGY: linear

(ii) MOLECULE TYPE: peptide

(v) FRAGMENT TYPE: internal

(ix) FEATURE:
(A) NAME/KEY: Peptide
(B) LOCATION: 1..8
(D) OTHER INFORMATION: /note= "30-37 REGION OF HUMAN IGF-I"

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:150:

Gly Tyr Gly Ser Ser Ser Arg Arg
1 5

(2) INFORMATION FOR SEQ ID NO:151:

(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 8 amino acids
(B) TYPE: amino acid
(D) TOPOLOGY: linear

(ii) MOLECULE TYPE: peptide

(v) FRAGMENT TYPE: internal

(ix) FEATURE:
(A) NAME/KEY: Peptide
(B) LOCATION: 1..8
(D) OTHER INFORMATION: /note= "31-38 REGION OF HUMAN IGF-I"

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:151:

Tyr Gly Ser Ser Ser Arg Arg Ala
1 5

(2) INFORMATION FOR SEQ ID NO:152:

(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 8 amino acids
(B) TYPE: amino acid
(D) TOPOLOGY: linear

(ii) MOLECULE TYPE: peptide

(v) FRAGMENT TYPE: internal

(ix) FEATURE:
(A) NAME/KEY: Peptide
(B) LOCATION: 1..8
(D) OTHER INFORMATION: /note= "32-39 REGION OF HUMAN IGF-I"

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:152:

Gly Ser Ser Ser Arg Arg Ala Pro
1 5

(2) INFORMATION FOR SEQ ID NO:153:

(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 8 amino acids
(B) TYPE: amino acid
(D) TOPOLOGY: linear

(ii) MOLECULE TYPE: peptide

(v) FRAGMENT TYPE: internal

(ix) FEATURE:
(A) NAME/KEY: Peptide
(B) LOCATION: 1..8
(D) OTHER INFORMATION: /note= "33-40 REGION OF HUMAN IGF-I"

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:153:

Ser Ser Ser Arg Arg Ala Pro Gln
1 5

(2) INFORMATION FOR SEQ ID NO:154:

(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 8 amino acids
(B) TYPE: amino acid
(D) TOPOLOGY: linear

(ii) MOLECULE TYPE: peptide

(v) FRAGMENT TYPE: internal

(ix) FEATURE:
(A) NAME/KEY: Peptide
(B) LOCATION: 1..8
(D) OTHER INFORMATION: /note= "34-41 REGION OF HUMAN IGF-I"

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:154:

Ser Ser Arg Arg Ala Pro Gln Thr
1 5

(2) INFORMATION FOR SEQ ID NO:155:

(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 8 amino acids
(B) TYPE: amino acid
(D) TOPOLOGY: linear

(ii) MOLECULE TYPE: peptide

(v) FRAGMENT TYPE: internal

(ix) FEATURE:
(A) NAME/KEY: Peptide
(B) LOCATION: 1..8
(D) OTHER INFORMATION: /note= "35-42 REGION OF HUMAN IGF-I"

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:155:

Ser Arg Arg Ala Pro Gln Thr Gly
1 5

(2) INFORMATION FOR SEQ ID NO:156:

(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 8 amino acids
(B) TYPE: amino acid
(D) TOPOLOGY: linear

(ii) MOLECULE TYPE: peptide

(v) FRAGMENT TYPE: internal

(ix) FEATURE:
(A) NAME/KEY: Peptide
(B) LOCATION: 1..8
(D) OTHER INFORMATION: /note= "36-43 REGION OF HUMAN IGF-I"

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:156:

Arg Arg Ala Pro Gln Thr Gly Ile
1 5

(2) INFORMATION FOR SEQ ID NO:157:

(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 8 amino acids
(B) TYPE: amino acid
(D) TOPOLOGY: linear

(ii) MOLECULE TYPE: peptide

(v) FRAGMENT TYPE: internal

(ix) FEATURE:
(A) NAME/KEY: Peptide
(B) LOCATION: 1..8
(D) OTHER INFORMATION: /note= "37-44 REGION OF HUMAN IGF-I"

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:157:

Arg Ala Pro Gln Thr Gly Ile Val
1 5

(2) INFORMATION FOR SEQ ID NO:158:

(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 8 amino acids
(B) TYPE: amino acid
(D) TOPOLOGY: linear

(ii) MOLECULE TYPE: peptide

(v) FRAGMENT TYPE: internal

(ix) FEATURE:
(A) NAME/KEY: Peptide
(B) LOCATION: 1..8
(D) OTHER INFORMATION: /note= "38-45 REGION OF HUMAN IGF-I"

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:158:

Ala Pro Gln Thr Gly Ile Val Asp
1 5

(2) INFORMATION FOR SEQ ID NO:159:

(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 8 amino acids
(B) TYPE: amino acid
(D) TOPOLOGY: linear

(ii) MOLECULE TYPE: peptide

(v) FRAGMENT TYPE: internal

(ix) FEATURE:
(A) NAME/KEY: Peptide
(B) LOCATION: 1..8
(D) OTHER INFORMATION: /note= "39-46 REGION OF HUMAN IGF-I"

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:159:

Pro Gln Thr Gly Ile Val Asp Glu
1 5

(2) INFORMATION FOR SEQ ID NO:160:

(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 8 amino acids
(B) TYPE: amino acid
(D) TOPOLOGY: linear

(ii) MOLECULE TYPE: peptide

(v) FRAGMENT TYPE: internal

(ix) FEATURE:
(A) NAME/KEY: Peptide
(B) LOCATION: 1..8
(D) OTHER INFORMATION: /note= "40-47 REGION OF HUMAN IGF-I"

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:160:

Gln Thr Gly Ile Val Asp Glu Cys
1 5

(2) INFORMATION FOR SEQ ID NO:161:

(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 8 amino acids
(B) TYPE: amino acid
(D) TOPOLOGY: linear

(ii) MOLECULE TYPE: peptide

(v) FRAGMENT TYPE: internal

(ix) FEATURE:
(A) NAME/KEY: Peptide
(B) LOCATION: 1..8
(D) OTHER INFORMATION: /note= "41-48 REGION OF HUMAN IGF-I"

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:161:

Thr Gly Ile Val Asp Glu Cys Cys
1 5

(2) INFORMATION FOR SEQ ID NO:162:

(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 8 amino acids
(B) TYPE: amino acid
(D) TOPOLOGY: linear

(ii) MOLECULE TYPE: peptide

(v) FRAGMENT TYPE: internal

(ix) FEATURE:
(A) NAME/KEY: Peptide
(B) LOCATION: 1..8
(D) OTHER INFORMATION: /note= "42-49 REGION OF HUMAN IGF-I"

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:162:

Gly Ile Val Asp Glu Cys Cys Phe
1 5

(2) INFORMATION FOR SEQ ID NO:163:

(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 8 amino acids
(B) TYPE: amino acid
(D) TOPOLOGY: linear

(ii) MOLECULE TYPE: peptide

(v) FRAGMENT TYPE: internal

(ix) FEATURE:
(A) NAME/KEY: Peptide
(B) LOCATION: 1..8
(D) OTHER INFORMATION: /note= "43-50 REGION OF HUMAN IGF-I"

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:163:

Ile Val Asp Glu Cys Cys Phe Arg
1 5

(2) INFORMATION FOR SEQ ID NO:164:

(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 8 amino acids
(B) TYPE: amino acid
(D) TOPOLOGY: linear

(ii) MOLECULE TYPE: peptide

(v) FRAGMENT TYPE: internal

(ix) FEATURE:
(A) NAME/KEY: Peptide
(B) LOCATION: 1..8
(D) OTHER INFORMATION: /note= "44-51 REGION OF HUMAN IGF-I"

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:164:

Val Asp Glu Cys Cys Phe Arg Ser
1 5

(2) INFORMATION FOR SEQ ID NO:165:

(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 8 amino acids
(B) TYPE: amino acid
(D) TOPOLOGY: linear

(ii) MOLECULE TYPE: peptide

(v) FRAGMENT TYPE: internal

(ix) FEATURE:
(A) NAME/KEY: Peptide
(B) LOCATION: 1..8
(D) OTHER INFORMATION: /note= "45-52 REGION OF HUMAN IGF-I"

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:165:

Asp Glu Cys Cys Phe Arg Ser Cys
1 5

(2) INFORMATION FOR SEQ ID NO:166:

(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 8 amino acids
(B) TYPE: amino acid
(D) TOPOLOGY: linear

(ii) MOLECULE TYPE: peptide

(v) FRAGMENT TYPE: internal

(ix) FEATURE:
(A) NAME/KEY: Peptide
(B) LOCATION: 1..8
(D) OTHER INFORMATION: /note= "46-53 REGION OF HUMAN IGF-I"

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:166:

Glu Cys Cys Phe Arg Ser Cys Asp
1 5

(2) INFORMATION FOR SEQ ID NO:167:

(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 8 amino acids
(B) TYPE: amino acid
(D) TOPOLOGY: linear

(ii) MOLECULE TYPE: peptide

(v) FRAGMENT TYPE: internal

(ix) FEATURE:
(A) NAME/KEY: Peptide
(B) LOCATION: 1..8
(D) OTHER INFORMATION: /note= "47-54 REGION OF HUMAN IGF-I"

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:167:

Cys Cys Phe Arg Ser Cys Asp Leu
1 5

(2) INFORMATION FOR SEQ ID NO:168:

(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 8 amino acids
(B) TYPE: amino acid
(D) TOPOLOGY: linear

(ii) MOLECULE TYPE: peptide

(v) FRAGMENT TYPE: internal

(ix) FEATURE:
(A) NAME/KEY: Peptide
(B) LOCATION: 1..8
(D) OTHER INFORMATION: /note= "48-55 REGION OF HUMAN IGF-I"

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:168:

Cys Phe Arg Ser Cys Asp Leu Arg
1 5

(2) INFORMATION FOR SEQ ID NO:169:

(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 8 amino acids
(B) TYPE: amino acid
(D) TOPOLOGY: linear

(ii) MOLECULE TYPE: peptide

(v) FRAGMENT TYPE: internal

(ix) FEATURE:
(A) NAME/KEY: Peptide
(B) LOCATION: 1..8
(D) OTHER INFORMATION: /note= "49-56 REGION OF HUMAN IGF-I"

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:169:

Phe Arg Ser Cys Asp Leu Arg Arg
1 5

(2) INFORMATION FOR SEQ ID NO:170:

(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 8 amino acids
(B) TYPE: amino acid
(D) TOPOLOGY: linear

(ii) MOLECULE TYPE: peptide

(v) FRAGMENT TYPE: internal

(ix) FEATURE:
(A) NAME/KEY: Peptide
(B) LOCATION: 1..8
(D) OTHER INFORMATION: /note= "50-57 REGION OF HUMAN IGF-I"

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:170:

Arg Ser Cys Asp Leu Arg Arg Leu
1 5

(2) INFORMATION FOR SEQ ID NO:171:

(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 8 amino acids
(B) TYPE: amino acid
(D) TOPOLOGY: linear

(ii) MOLECULE TYPE: peptide

(v) FRAGMENT TYPE: internal

(ix) FEATURE:
(A) NAME/KEY: Peptide
(B) LOCATION: 1..8
(D) OTHER INFORMATION: /note= "51-58 REGION OF HUMAN IGF-I"

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:171:

Ser Cys Asp Leu Arg Arg Leu Glu
1 5

(2) INFORMATION FOR SEQ ID NO:172:

(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 8 amino acids
(B) TYPE: amino acid
(D) TOPOLOGY: linear

(ii) MOLECULE TYPE: peptide

(v) FRAGMENT TYPE: internal

(ix) FEATURE:
(A) NAME/KEY: Peptide
(B) LOCATION: 1..8
(D) OTHER INFORMATION: /note= "52-59 REGION OF HUMAN IGF-I"

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:172:

Cys Asp Leu Arg Arg Leu Glu Met
1 5

(2) INFORMATION FOR SEQ ID NO:173:

(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 8 amino acids
(B) TYPE: amino acid
(D) TOPOLOGY: linear

(ii) MOLECULE TYPE: peptide

(v) FRAGMENT TYPE: internal

(ix) FEATURE:
(A) NAME/KEY: Peptide
(B) LOCATION: 1..8
(D) OTHER INFORMATION: /note= "53-60 REGION OF HUMAN IGF-I"

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:173:

Asp Leu Arg Arg Leu Glu Met Tyr
1 5

(2) INFORMATION FOR SEQ ID NO:174:

(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 8 amino acids
(B) TYPE: amino acid
(D) TOPOLOGY: linear

(ii) MOLECULE TYPE: peptide

(v) FRAGMENT TYPE: internal

(ix) FEATURE:
(A) NAME/KEY: Peptide
(B) LOCATION: 1..8
(D) OTHER INFORMATION: /note= "54-61 REGION OF HUMAN IGF-I"

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:174:

Leu Arg Arg Leu Glu Met Tyr Cys
1 5

(2) INFORMATION FOR SEQ ID NO:175:

(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 8 amino acids
(B) TYPE: amino acid
(D) TOPOLOGY: linear

(ii) MOLECULE TYPE: peptide

(v) FRAGMENT TYPE: internal

(ix) FEATURE:
(A) NAME/KEY: Peptide
(B) LOCATION: 1..8
(D) OTHER INFORMATION: /note= "55-62 REGION OF HUMAN IGF-I"

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:175:

Arg Arg Leu Glu Met Tyr Cys Ala
1 5

(2) INFORMATION FOR SEQ ID NO:176:

(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 8 amino acids
(B) TYPE: amino acid
(D) TOPOLOGY: linear

(ii) MOLECULE TYPE: peptide

(v) FRAGMENT TYPE: internal

(ix) FEATURE:
(A) NAME/KEY: Peptide
(B) LOCATION: 1..8
(D) OTHER INFORMATION: /note= "56-63 REGION OF HUMAN IGF-I"

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:176:

Arg Leu Glu Met Tyr Cys Ala Pro
1 5

(2) INFORMATION FOR SEQ ID NO:177:

(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 8 amino acids
(B) TYPE: amino acid
(D) TOPOLOGY: linear

(ii) MOLECULE TYPE: peptide

(v) FRAGMENT TYPE: internal

(ix) FEATURE:
(A) NAME/KEY: Peptide
(B) LOCATION: 1..8
(D) OTHER INFORMATION: /note= "57-64 REGION OF HUMAN IGF-I"

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:177:

Leu Glu Met Tyr Cys Ala Pro Leu
1 5

CLAIMS

1. A specific binding molecule, other than a natural IGF binding protein, which is capable of binding to insulin-like growth factor-I (IGF-I) and which is capable of enhancing a biological activity of IGF-I.

2. A specific binding molecule as claimed in claim 1, which is an antibody or is derived from an antibody.

3. A specific binding molecule as claimed in claim 2, which is a monoclonal antibody.

4. A specific binding molecule as claimed in claim 2, which is a humanised antibody.

5. A specific binding molecule as claimed in any one of claims 1 to 4, wherein the biological activity of IGF-I is an IGF-I-mediated anabolic action of growth hormone.

6. A specific binding molecule as claimed in any one of claims 1 to 5, which is capable of enhancing at least one of the following biological activities of IGF-I:

Increasing whole body and muscle growth rate in normal and hypopituitary animals;
Protection of body weight and nitrogen loss during catabolic states (such as fasting, nitrogen restriction, elevated corticosteroid levels and/or diabetes);
Kidney regeneration;
Nerve regeneration;
Hypoxia;
Wound healing;

Cardiac regeneration;
Cancer cachexia;
Angiogenesis;
Regeneration of the gastrointestinal tract;
Stimulation of mammary function;
IGF-I-dependent actions of GH (such as, usefulness in metabolic stress, age-related decreases in GH activity and adult GH deficiency);
Usefulness in maturity-onset diabetes; and/or
Usefulness in specific IGF-I deficiency.

7. A specific binding molecule as claimed in any one of claims 1 to 6, which binds to at least part of the region encompassing residues 1 to 17 of IGF-I.

8. A specific binding molecule which is capable of binding to insulin-like growth factor-I (IGF-I) and which is capable of enhancing a biological activity of IGF-I, for use in medicine.

9. An antigenic molecule which is capable, upon administration to a subject, of causing the generation of antibodies, wherein the antibodies are capable of binding to insulin-like growth factor-I (IGF-I) and of enhancing a biological activity of IGF-I.

10. An antigenic molecule as claimed in claim 9, which causes antibodies to be raised against a region encompassing at least some of residues 1 to 17, 18 to 21, 22 to 37, 36 to 44, 45 to 53, 54 to 60, or 59 to 70, of IGF-I.

11. An antigenic molecule as claimed in claim 10, which comprises at least some of residues 36 to 44 of IGF-I.

12. A pharmaceutical formulation comprising a molecule as claimed in any one of claims 1 to 11 and a pharmaceutically acceptable carrier.

13. A product comprising IGF-I and a molecule as claimed in any one of claims 1 to 11 for simultaneous, separate or sequential use in therapy in which IGF-I is useful.

14. The use of a molecule as claimed in any one of claims 1 to 11 in the manufacture of a medicament for treating or preventing conditions in which IGF-I is useful.

Fig. 1a.

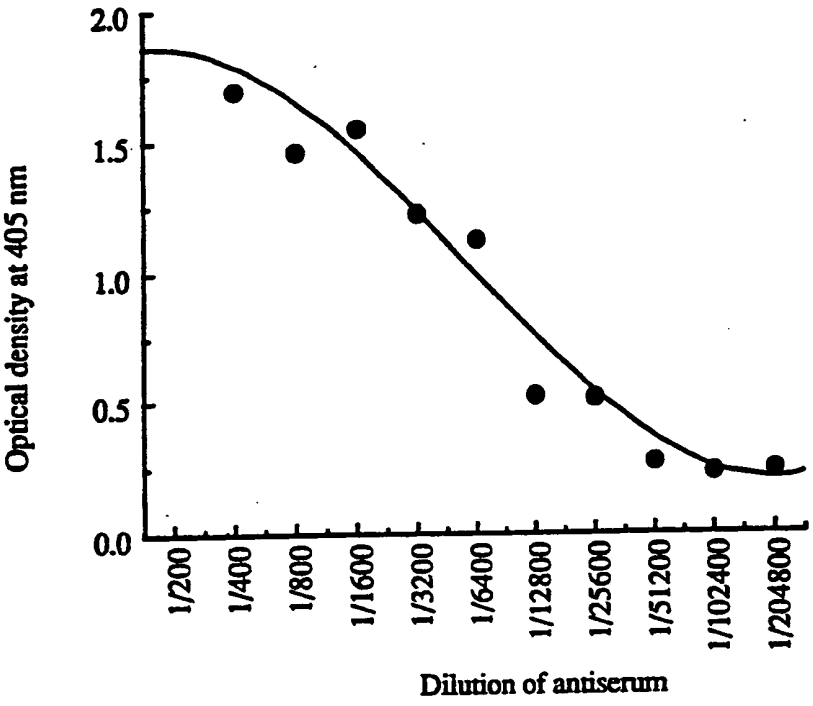

2.0
1.5
1.0
0.5
0.0
Optical density at 405 nm
1/200
1/400
1/800
1/1600
1/3200
1/6400
1/12800
1/25600
1/51200
1/102400
1/204800
Dilution of antiserum

Fig. 1b.

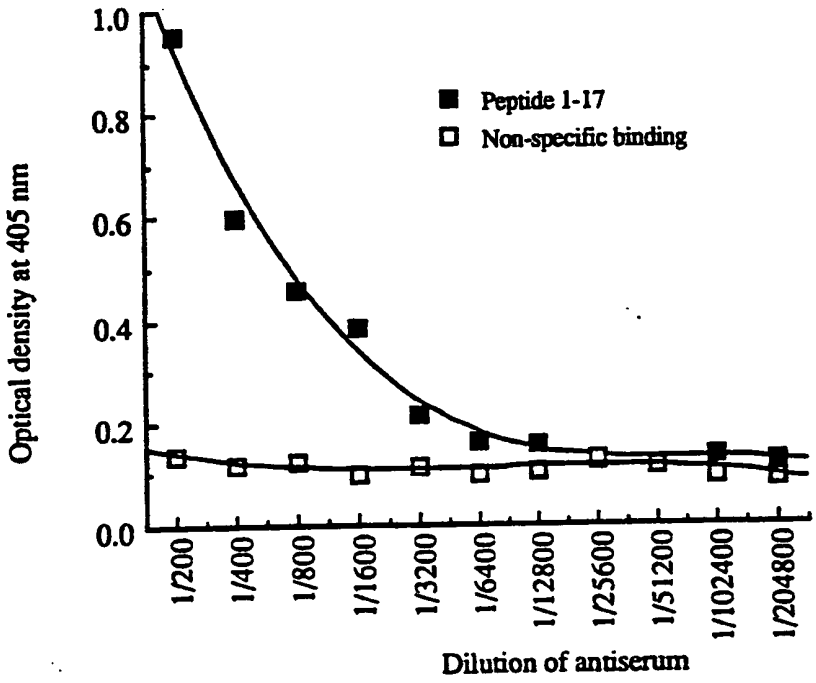

1.0
0.8
0.6
0.4
0.2
0.0
Optical density at 405 nm
Peptide 1-17
Non-specific binding
1/200
1/400
1/800
1/1600
1/3200
1/6400
1/12800
1/25600
1/51200
1/102400
1/204800
Dilution of antiserum

Fig. 1c.

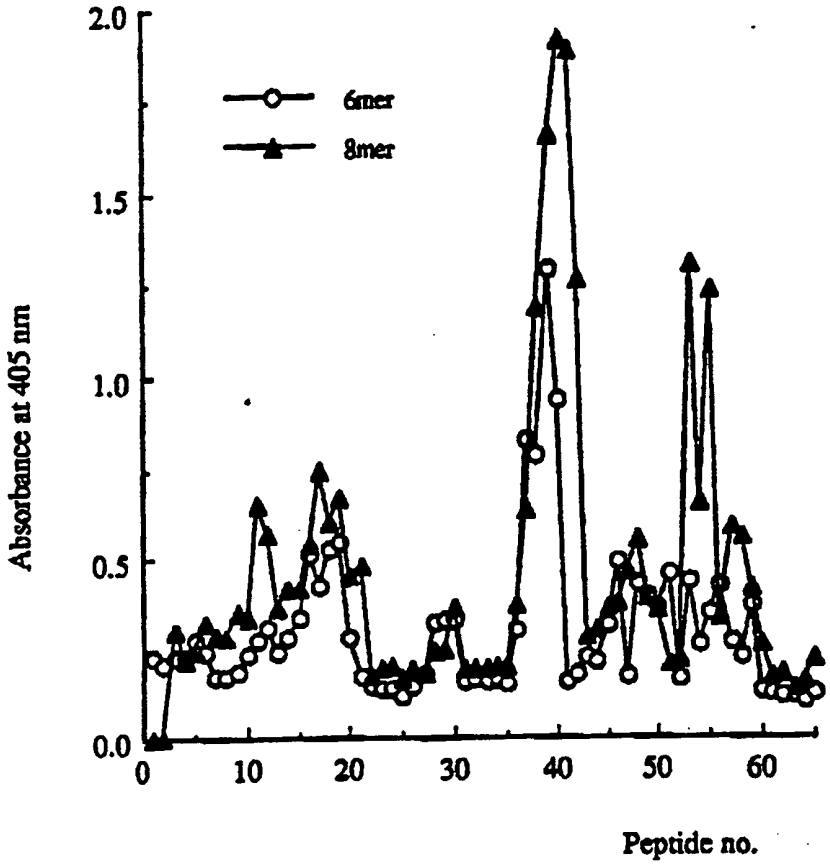

2.0
1.5
1.0
0.5
0.0
Absorbance at 405 nm
6mer
8mer
0
10
20
30
40
50
60
Peptide no.

Fig. 2.

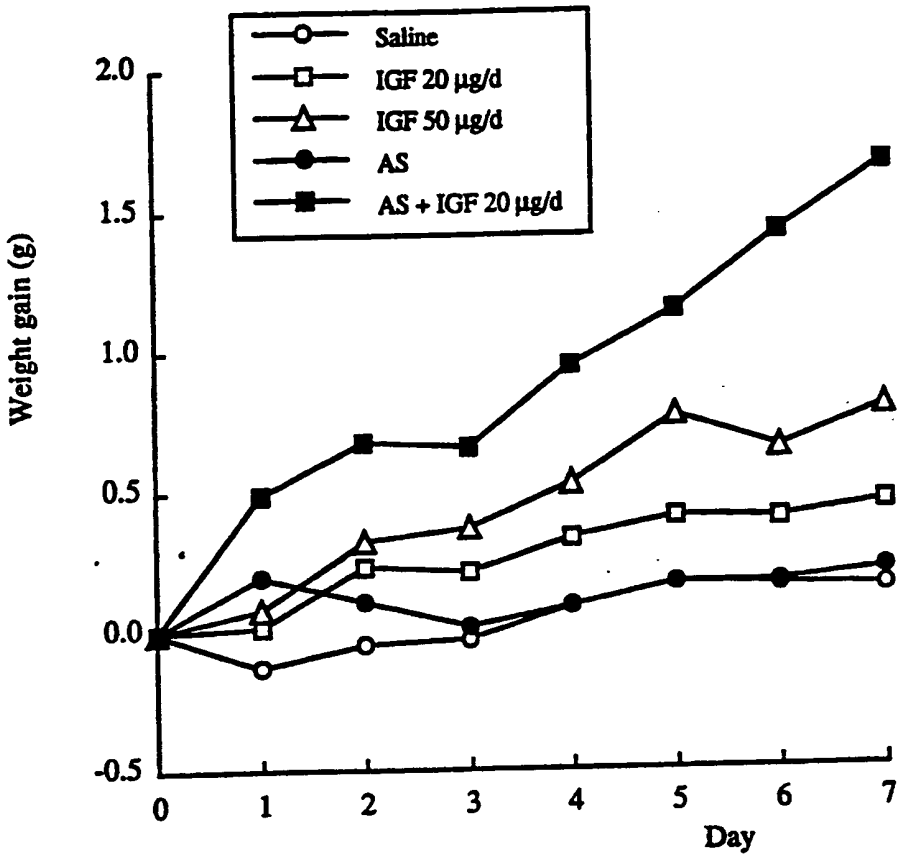

Saline
IGF 20 µg/d
IGF 50 µg/d
AS
AS + IGF 20 µg/d
Weight gain (g)
2.0
1.5
1.0
0.5
0.0
-0.5
0
1
2
3
4
5
6
7
Day

Fig. 3.

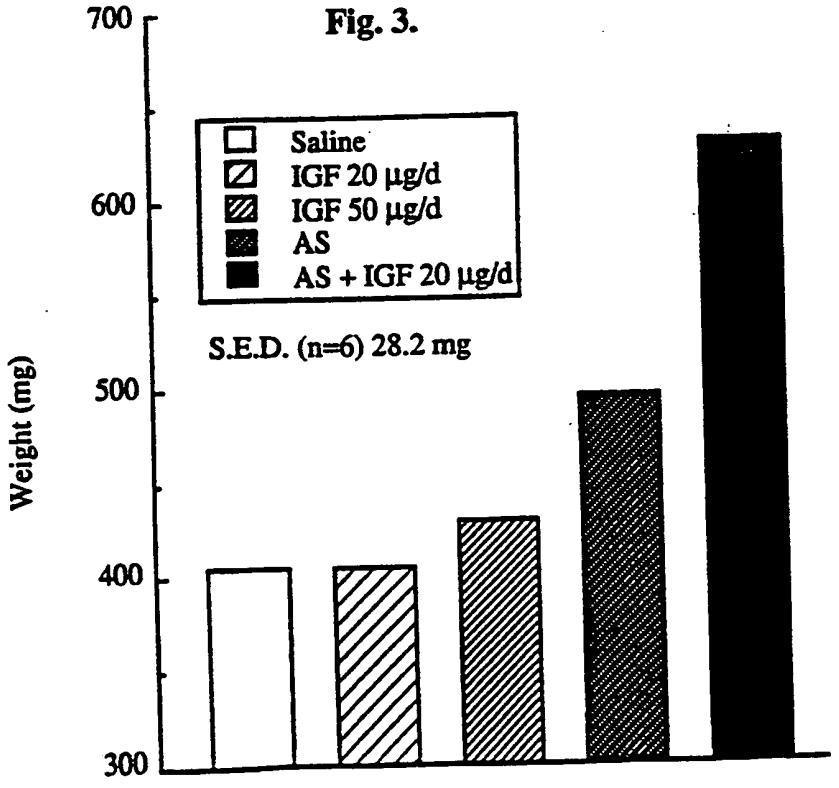

Saline
IGF 20 µg/d
IGF 50 µg/d
AS
AS + IGF 20 µg/d
S.E.D. (n=6) 28.2 mg
Weight (mg)
700
600
500
400
300

Fig. 4.

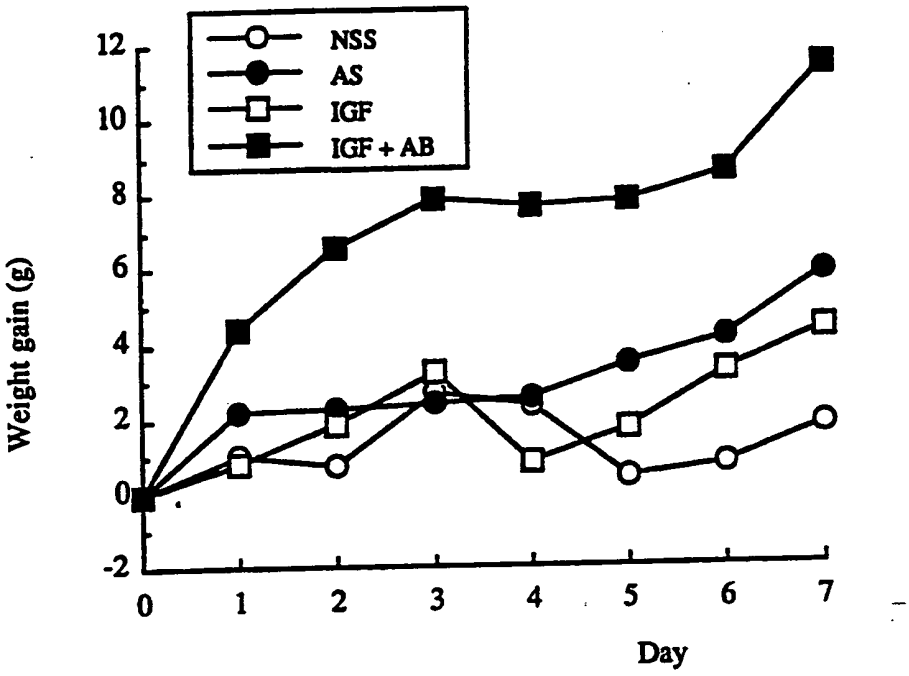

NSS
AS
IGF
IGF + AB
Weight gain (g)
12
10
8
6
4
2
0
-2
0
1
2
3
4
5
6
7
Day

Fig. 5.

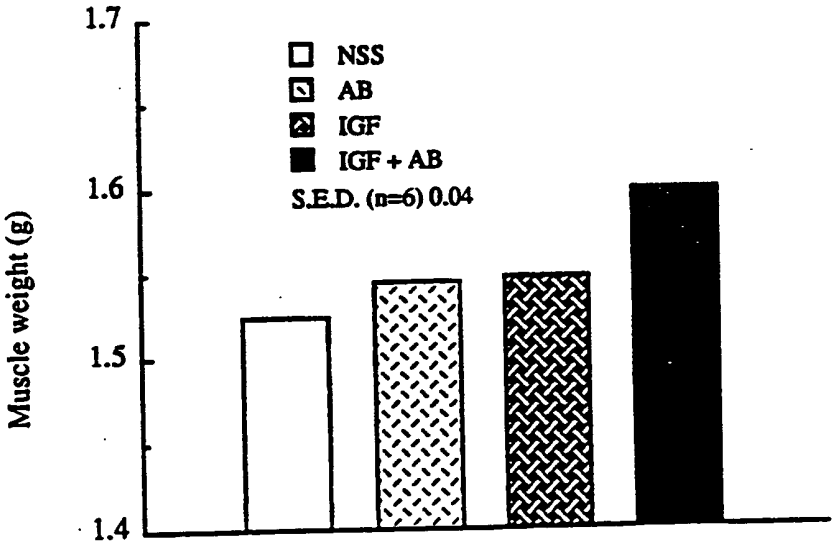

NSS
AB
IGF
IGF + AB
S.E.D. (n=6) 0.04
Muscle weight (g)
1.7
1.6
1.5
1.4

Fig. 6.

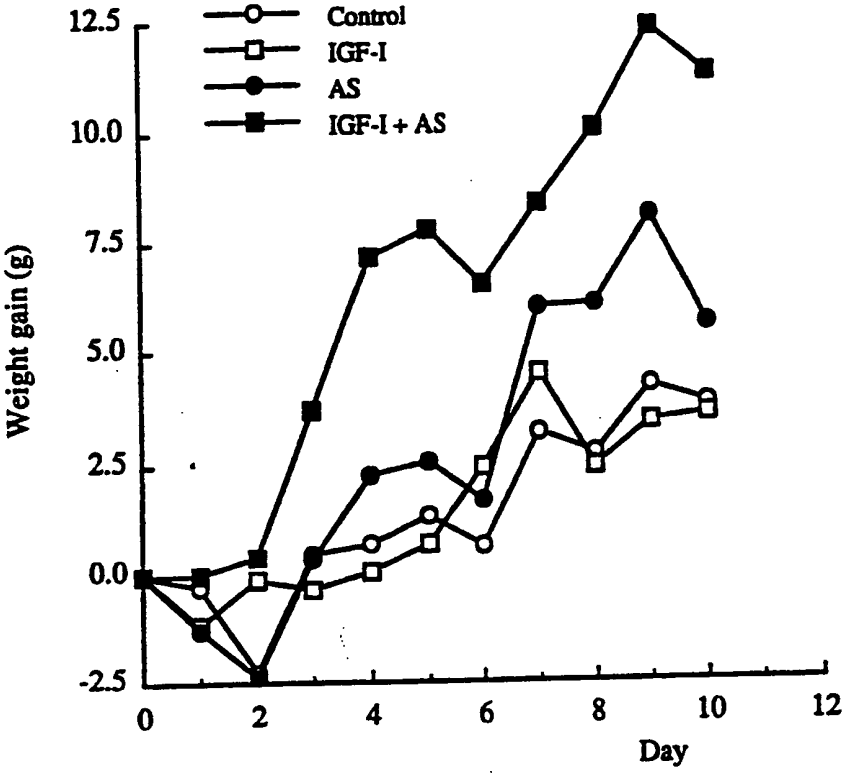
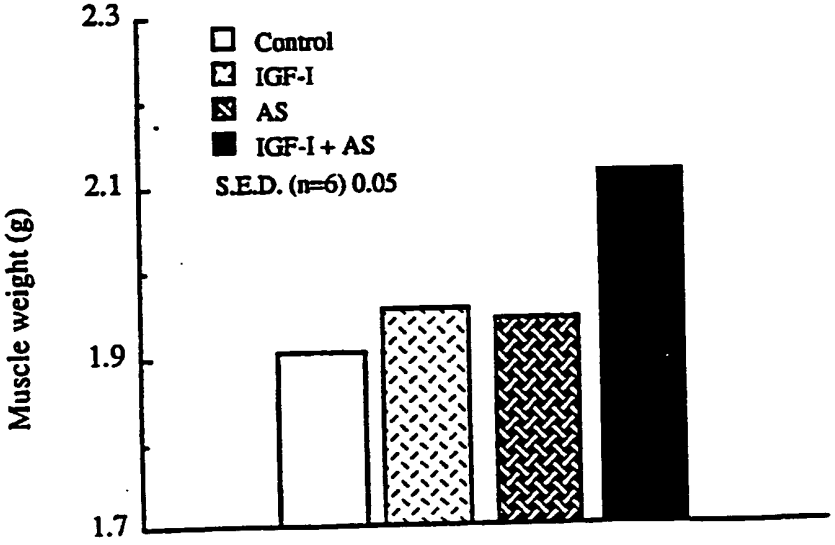

Control
IGF-I
AS
IGF-I + AS
12.5
10.0
7.5
5.0
2.5
0.0
-2.5
Weight gain (g)
0
2
4
6
8
10
12
Day

Fig. 7.


Control
IGF-I
AS
IGF-I + AS
S.E.D. (n=6) 0.05
2.3
2.1
1.9
1.7
Muscle weight (g)

A. CLASSIFICATION OF SUBJECT MATTER
IPC 5 C07K15/06 C12P21/08 A61K39/395 C07K7/06 C07K7/08
A61K39/00 A61K37/02 //(A61K39/395,37:02)

According to International Patent Classification (IPC) or to both national classification and IPC

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)
IPC 5 C07K C12P A61K

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practical, search terms used)

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
A	GENE. vol. 58, no. 1 , 1987 , AMSTERDAM NL pages 87 - 97 B. LÖWENADLER ET AL. 'A GENE FUSION SYSTEM FOR GENERATING ANTIBODIES AGAINST SHORT PEPTIDES.' see the whole document ---	1-14
A	PROCEEDINGS OF THE NATIONAL ACADEMY OF SCIENCES OF USA. vol. 84 , May 1987 , WASHINGTON US pages 3254 - 3258 R.G. ELGIN ET AL. 'AN INSULIN-LIKE GROWTH FACTOR (IGF) BINDING PROTEIN ENHANCES THE BIOLOGIC RESPONSE TO IGF-I.' cited in the application see the whole document --- -/--	1-14

[X] Further documents are listed in the continuation of box C.

[ ] Patent family members are listed in annex.

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"&" document member of the same patent family

Date of the actual completion of the international search	Date of mailing of the international search report
10 December 1993	22 -12- 1993

Name and mailing address of the ISA	Authorized officer
European Patent Office, P.B. 5818 Patentlaan 2 NL - 2280 HV Rijswijk Tel. (+31-70) 340-2040, Tx. 31 651 epo nl, Fax (+31-70) 340-3016	Ryckebosch, A

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C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
A	CHEMICAL ABSTRACTS, vol. 114, no. 21, 27 May 1991, Columbus, Ohio, US; abstract no. 200433c, G.S.G. SPENCER ET AL. 'PASSIVE IMMUNIZATION AGAINST INSULIN-LIKE GROWTH FACTOR-1 DOES NOT INHIBIT GROWTH HORMONE-STIMULATED GROWTH OF DWARF RATS.' page 175 ; cited in the application see abstract & ENDOCRINOLOGY (BALTIMORE) vol. 128, no. 4 , 1991 pages 2103 - 2109	1-14
A	CHEMICAL ABSTRACTS, vol. 115, no. 19, 11 November 1991, Columbus, Ohio, US; abstract no. 199067y, J.M. PELL ET AL. 'ACTIVE IMMUNIZATION WITH A SYNTHETIC PEPTIDE REGION OF GROWTH HORMONE: INCREASED LEAN TISSUE GROWTH.' page 157 ; see abstract & J. ENDOCRINOL. vol. 131, no. 1 , 1991 pages R1 - R4	1-14